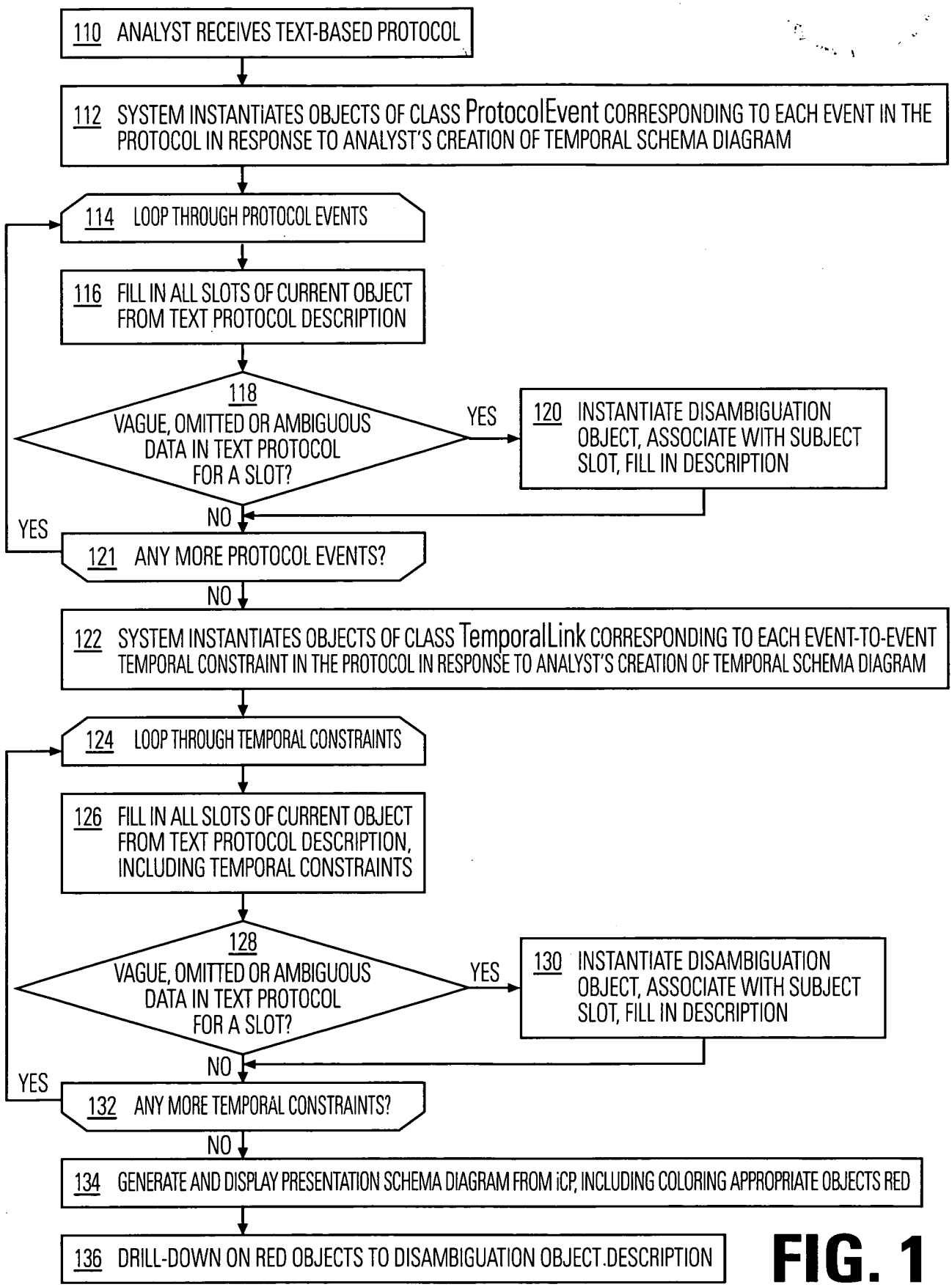

FIG. 1

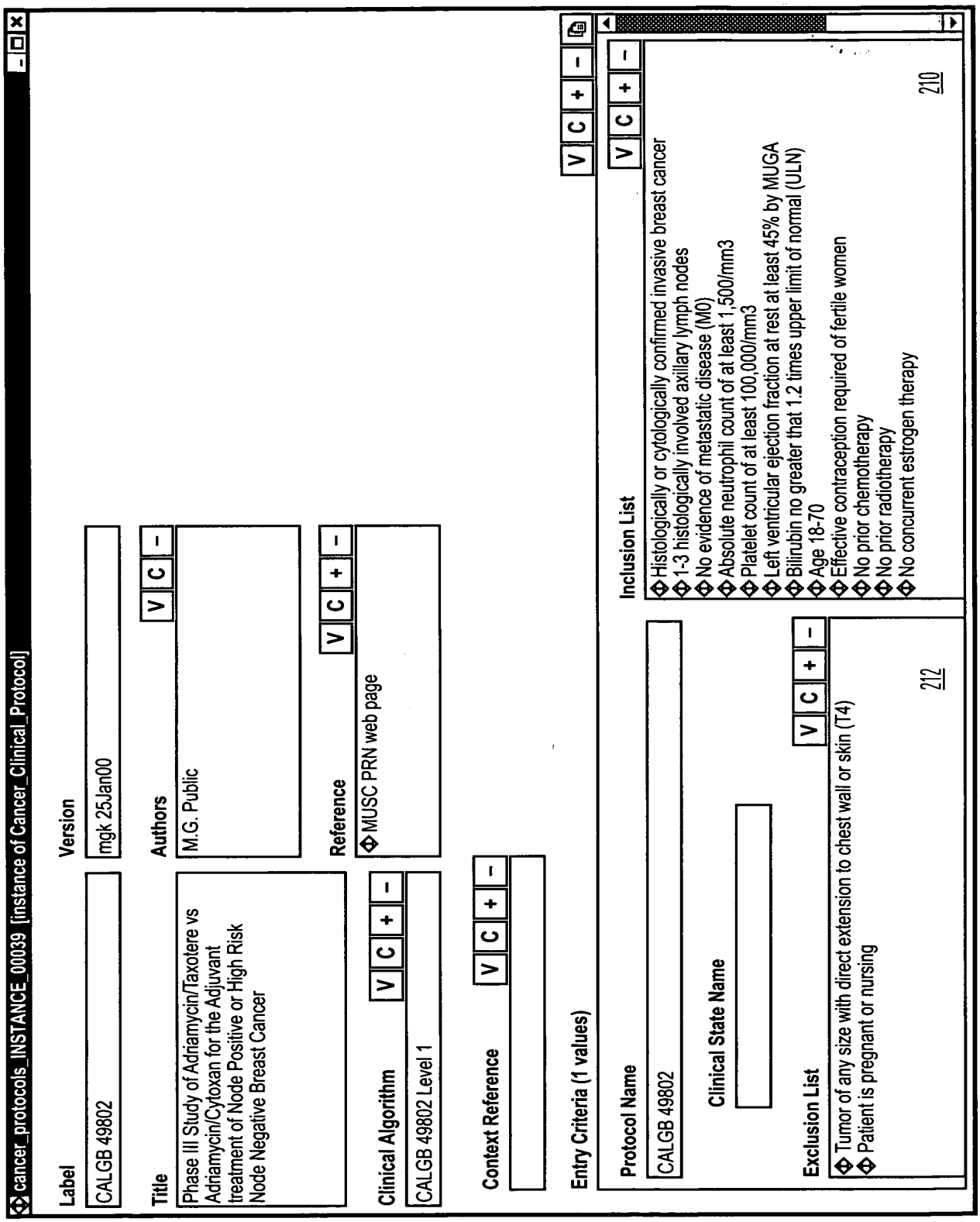

FIG. 2

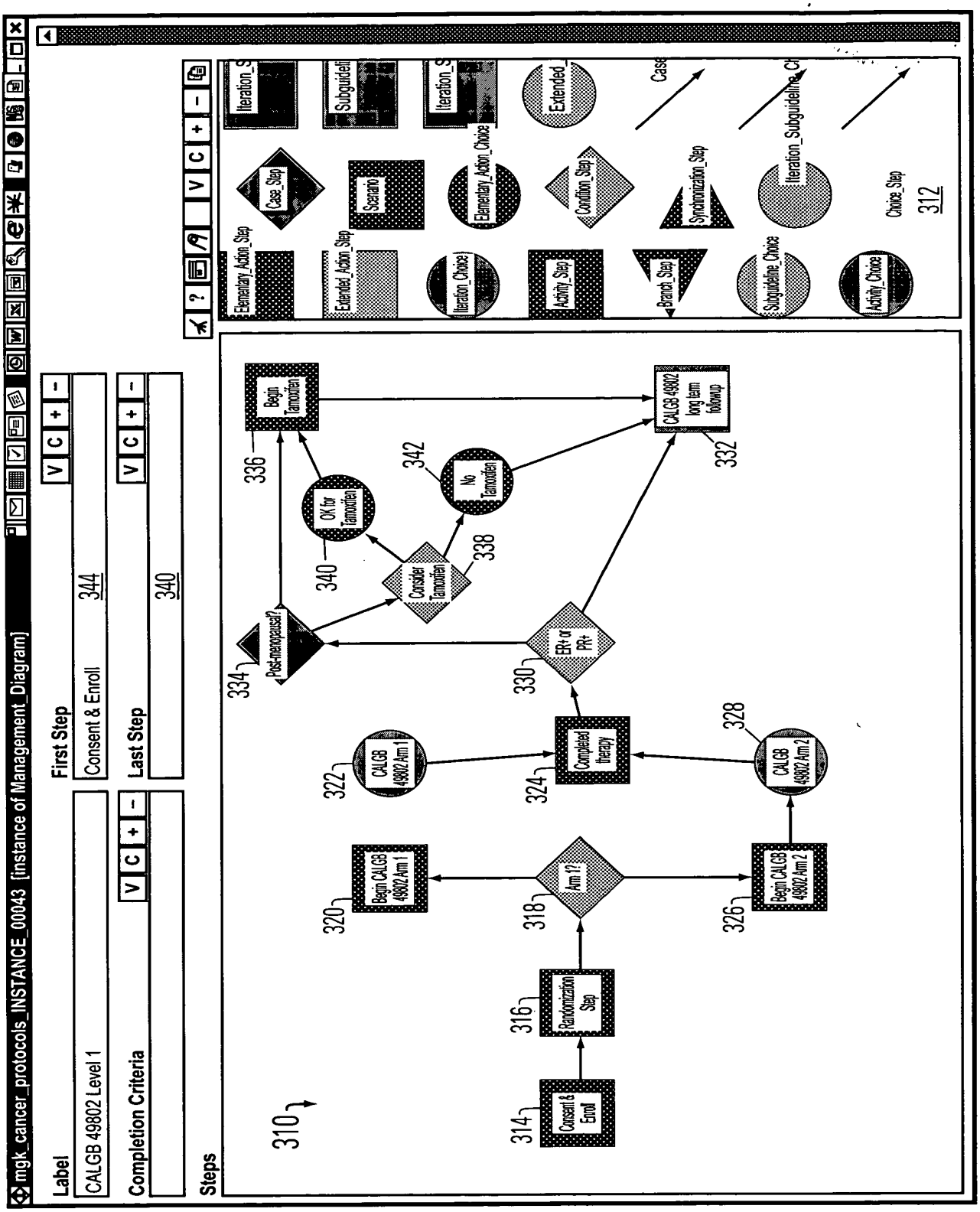
mgk_cancer_protocols_INSTANCE_00043 [instance of Management_Diagram]
Label
CALGB 49802 Level 1
First Step
Consent & Enroll
344
Completion Criteria
Last Step
340
Steps
310
Consent & Enrol
314
Randomization Step
316
Arm 1?
318
Begin CALGB 49802 Arm 1
320
CALGB 49802 Arm 1
322
Completed therapy
324
Begin CALGB 49802 Arm 2
326
CALGB 49802 Arm 2
328
ER+ or PR+
330
CALGB 49802 long term followup
332
Post-menopause?
334
Consider Tamoxifen
338
OK for Tamoxifen
340
No Tamoxifen
342
Begin Tamoxifen
336
Elementary_Action_Step
Extended_Action_Step
Case_Step
Scenario
Iteration_Choice
Elementary_Action_Choice
Activity_Step
Condition_Step
Branch_Step
Synchronization_Step
Subguideline_Choice
Iteration_Subguideline_Ch
Activity_Choice
Choice_Step
312

FIG. 3

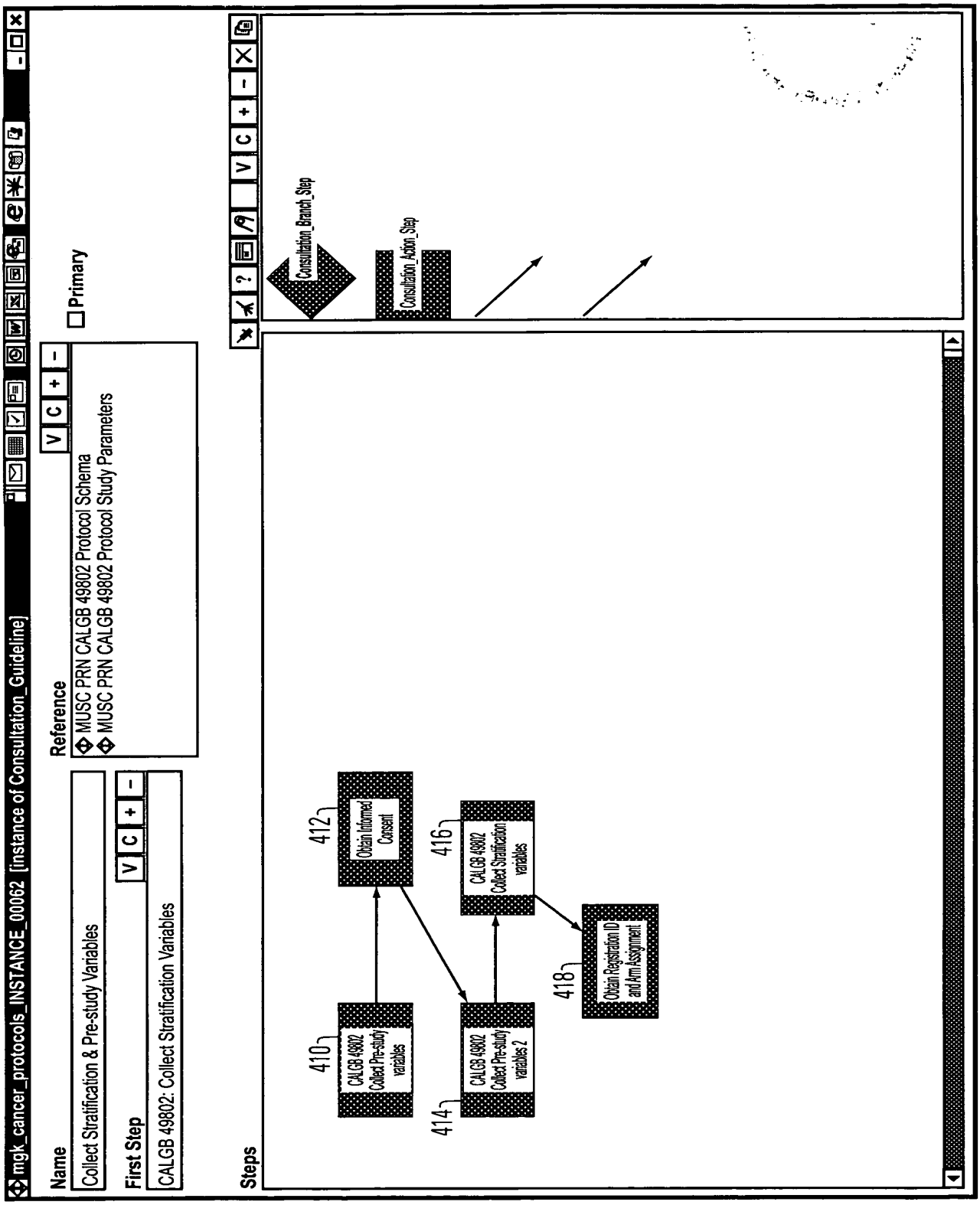
mgk_cancer_protocols_INSTANCE_00062 [instance of Consultation_Guideline]
Name
Collect Stratification & Pre-study Variables
First Step
CALGB 49802: Collect Stratification Variables
Reference
MUSC PRN CALGB 49802 Protocol Schema
MUSC PRN CALGB 49802 Protocol Study Parameters
Primary
Steps
Consultation_Branch_Step
Consultation_Action_Step
412
Obtain Informed Consent
410
CALGB 49802 Collect Pre-study variables
414
CALGB 49802 Collect Pre-study variables 2
416
CALGB 49802 Collect Stratification variables
418
Obtain Registration ID and Arm Assignment

FIG. 4

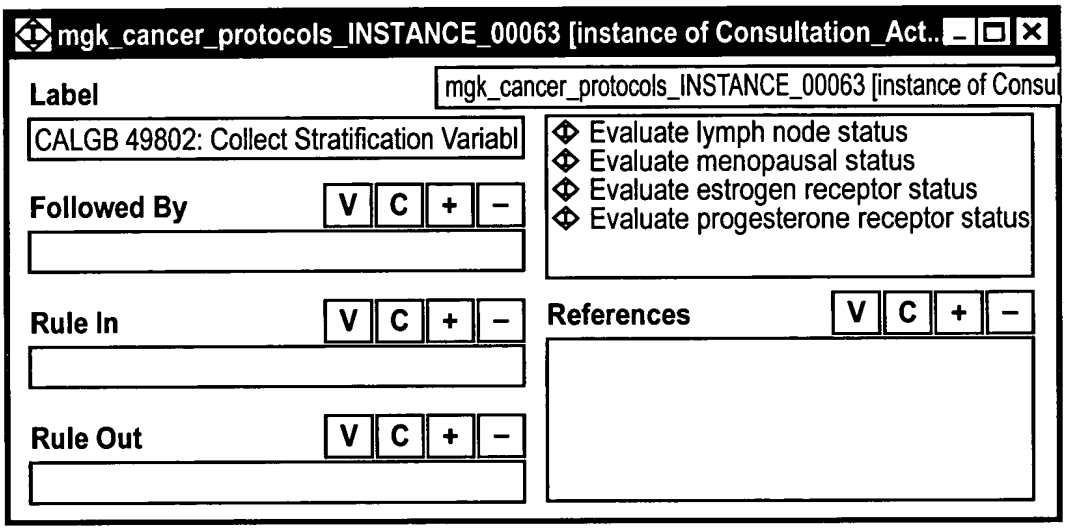
mgk_cancer_protocols_INSTANCE_00063 [instance of Consultation_Act..
Label
mgk_cancer_protocols_INSTANCE_00063 [instance of Consul
CALGB 49802: Collect Stratification Variabl
Evaluate lymph node status
Evaluate menopausal status
Evaluate estrogen receptor status
Evaluate progesterone receptor status
Followed By
V C + −
Rule In
V C + −
References
V C + −
Rule Out
V C + −

FIG. 5

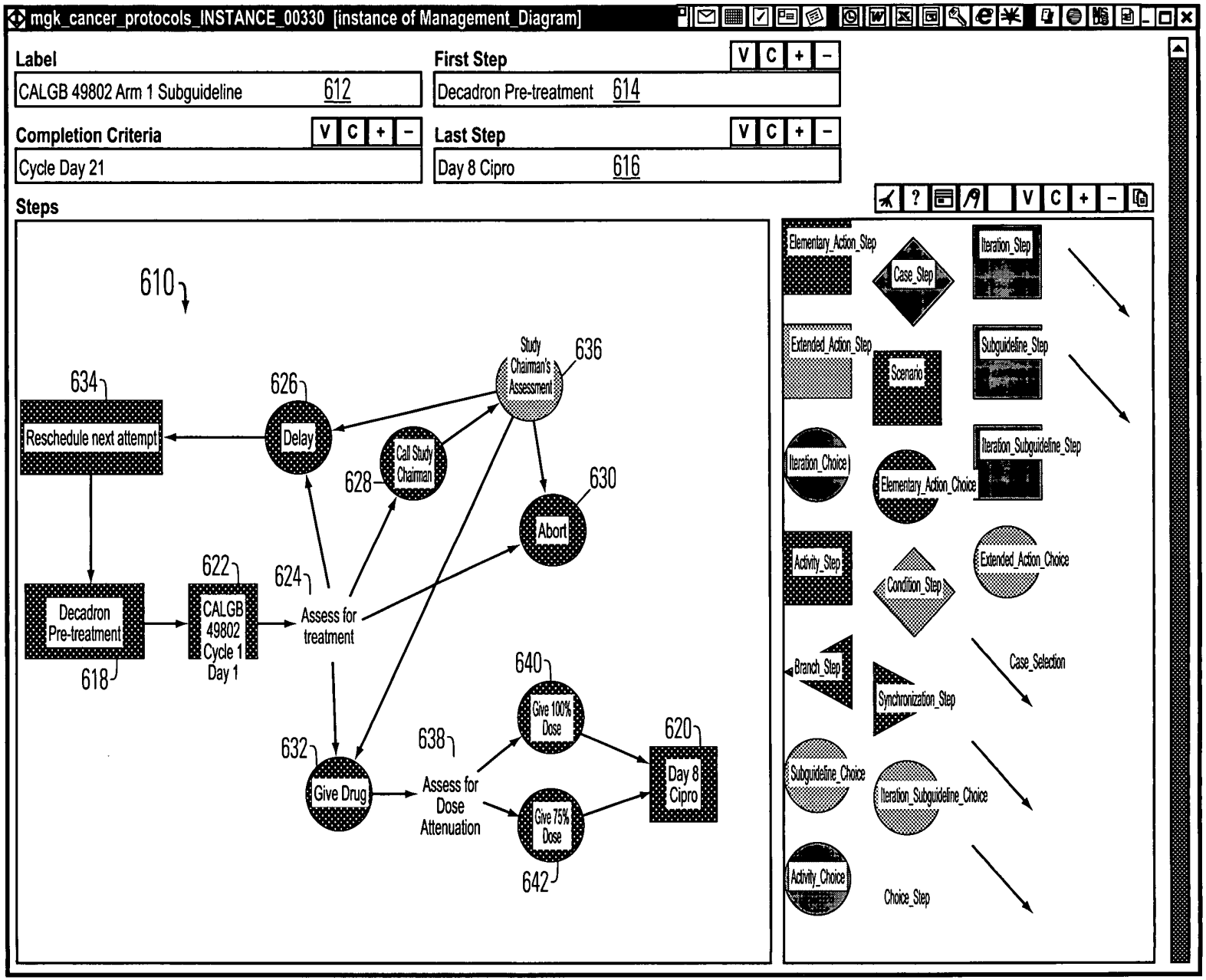

FIG. 6

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

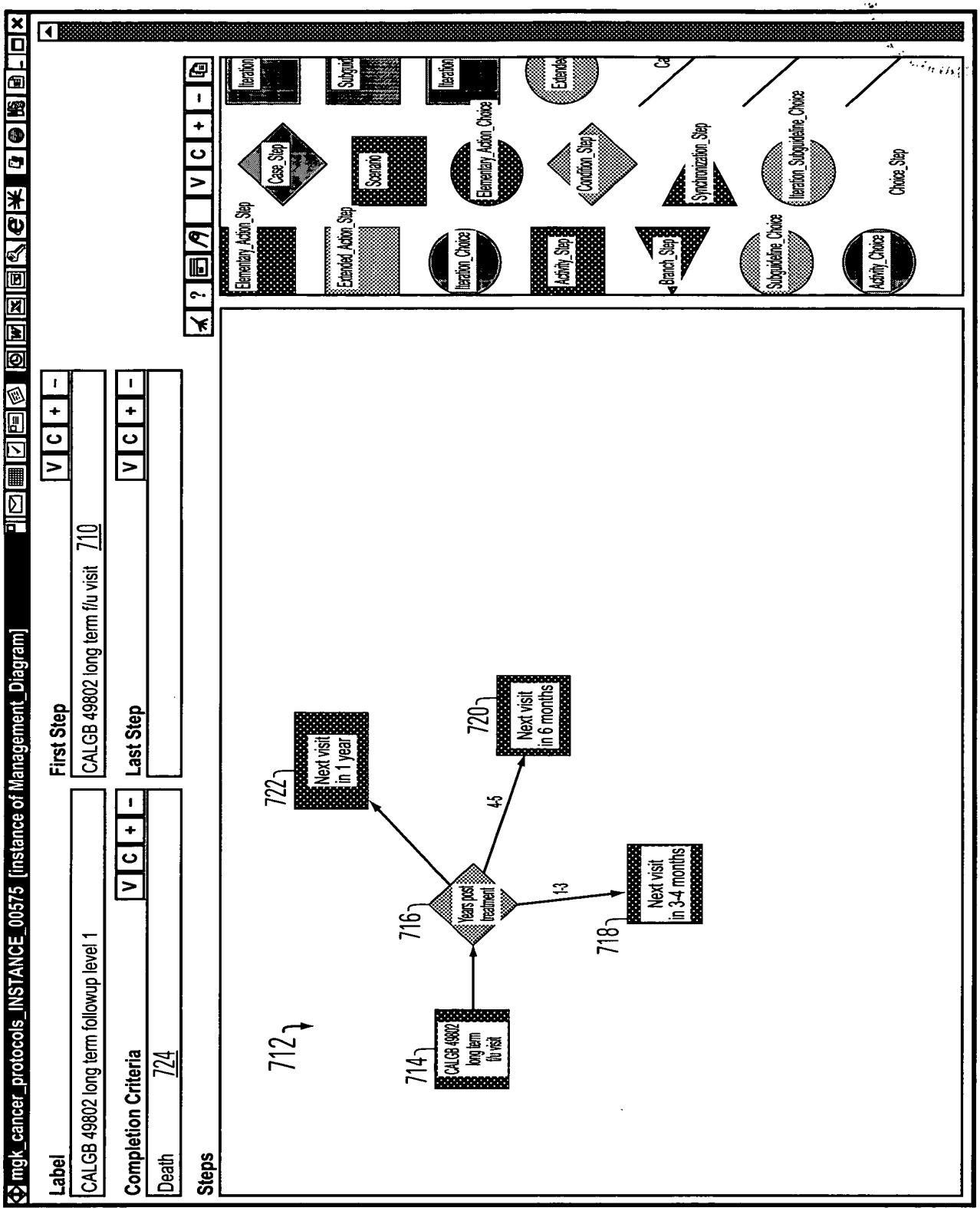
mgk_cancer_protocols_INSTANCE_00575 (instance of Management_Diagram)
Label
CALGB 49802 long term followup level 1
Completion Criteria
Death 724
Steps
First Step
CALGB 49802 long term f/u visit 710
Last Step
Elementary_Action_Step
Extended_Action_Step
Iteration_Choice
Activity_Step
Branch_Step
Case_Step
Scenario
Elementary_Action_Step
Condition_Step
Synchronization_Step
Iteration_Subguideline_Choice
Choice_Step
712
714
CALGB 49802 long term f/u visit
716
Years post treatment
45
1-3
718
Next visit in 3-4 months
720
Next visit in 6 months
722
Next visit in 1 year

FIG. 7

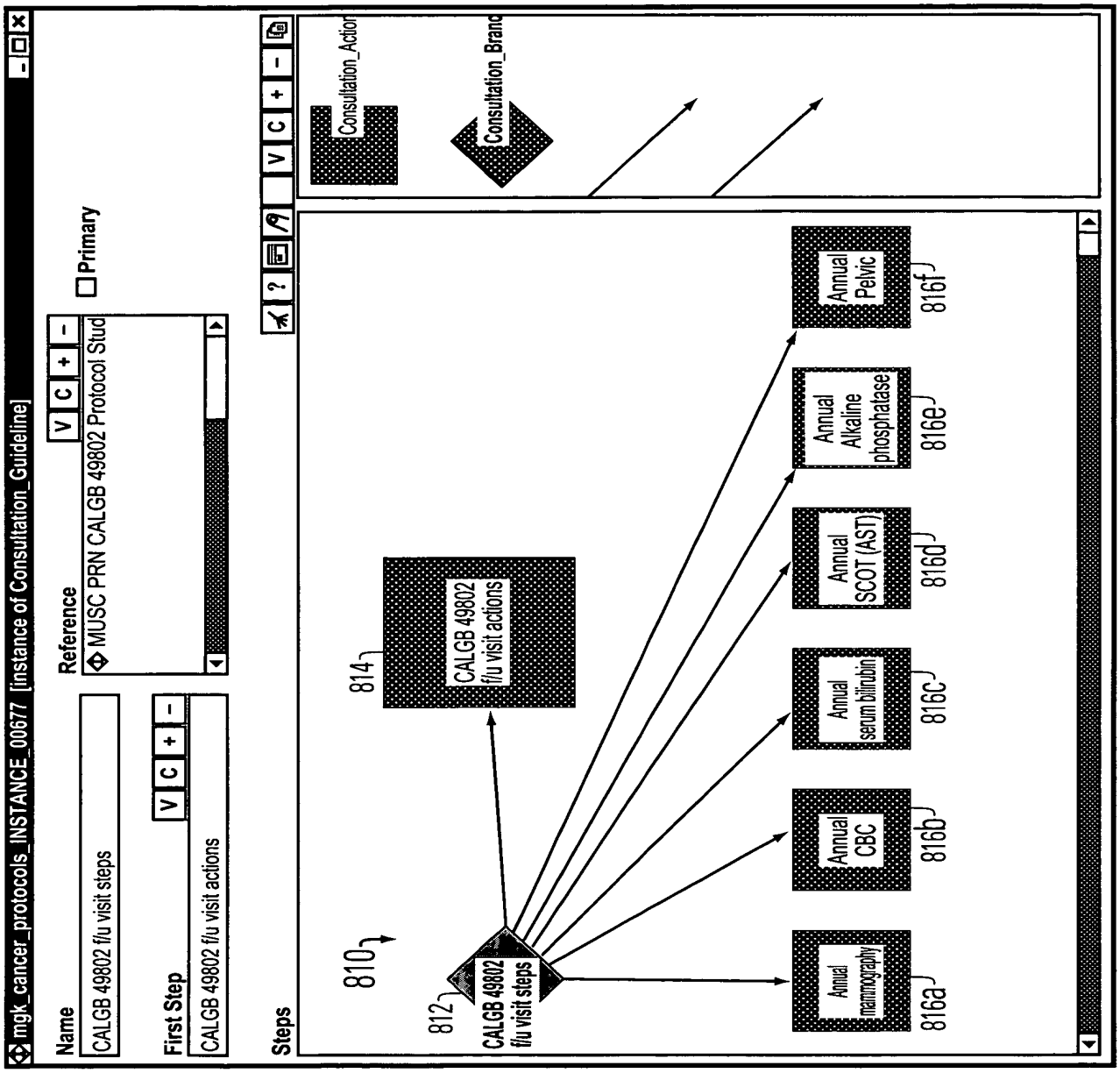
mgk_cancer_protocols_INSTANCE_00677 [instance of Consultation_Guideline]
Name
CALGB 49802 f/u visit steps
Reference
MUSC PRN CALGB 49802 Protocol Stud
Primary
First Step
CALGB 49802 f/u visit actions
Steps
Consultation_Actior
Consultation_Brand
810
812
CALGB 49802 f/u visit steps
814
CALGB 49802 f/u visit actions
816a
Annual mammography
816b
Annual CBC
816c
Annual serum bilirubin
816d
Annual SCOT (AST)
816e
Annual Alkaline phosphatase
816f
Annual Pelvic

FIG. 8

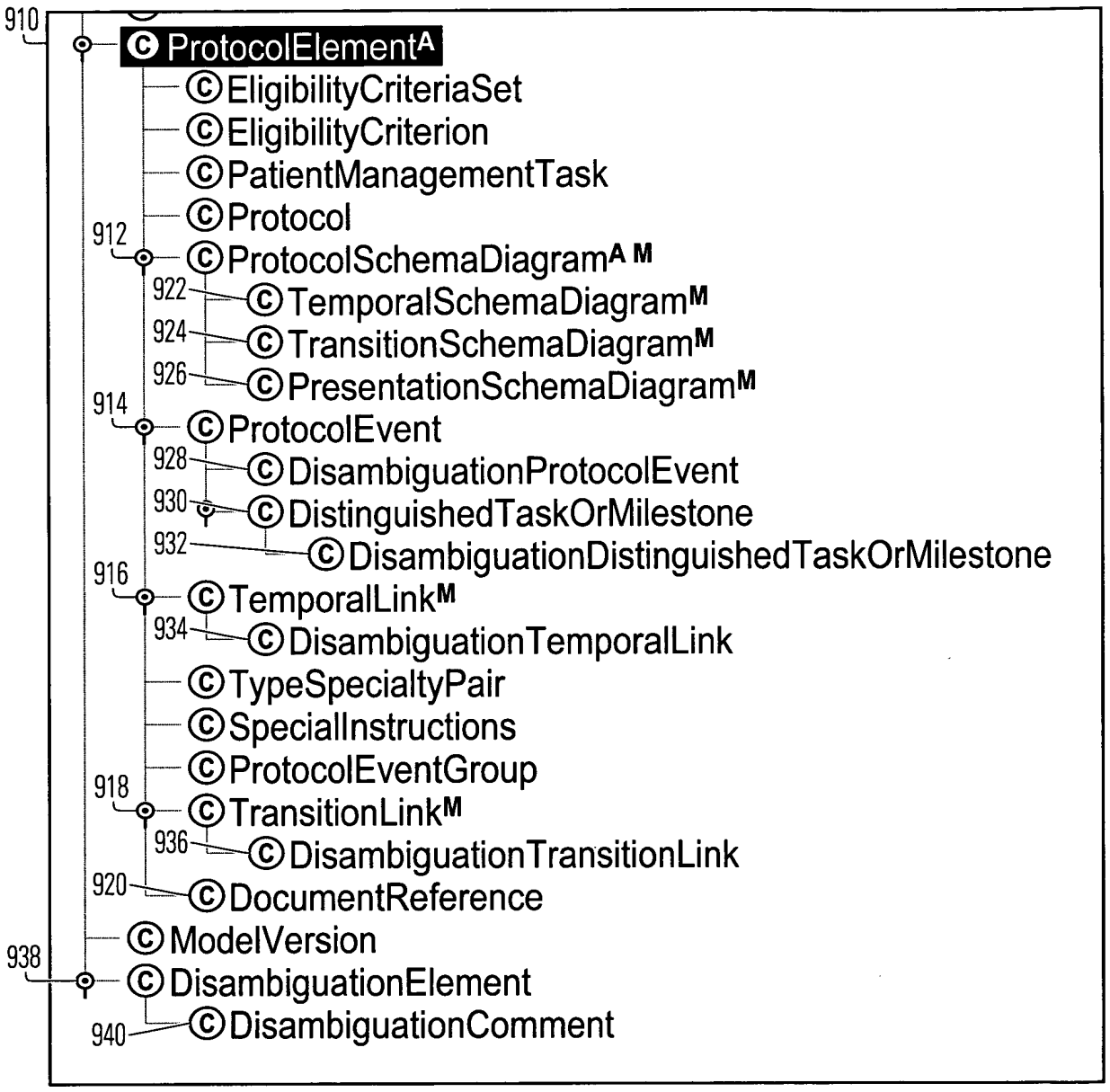

FIG. 9

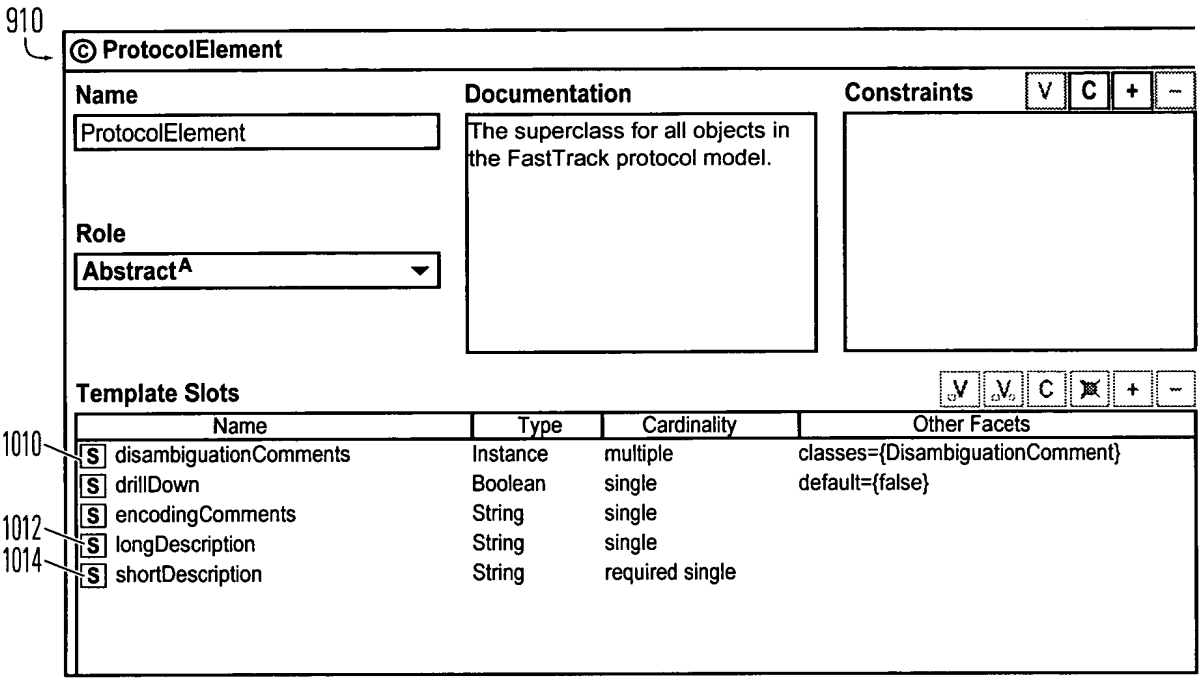

FIG. 10

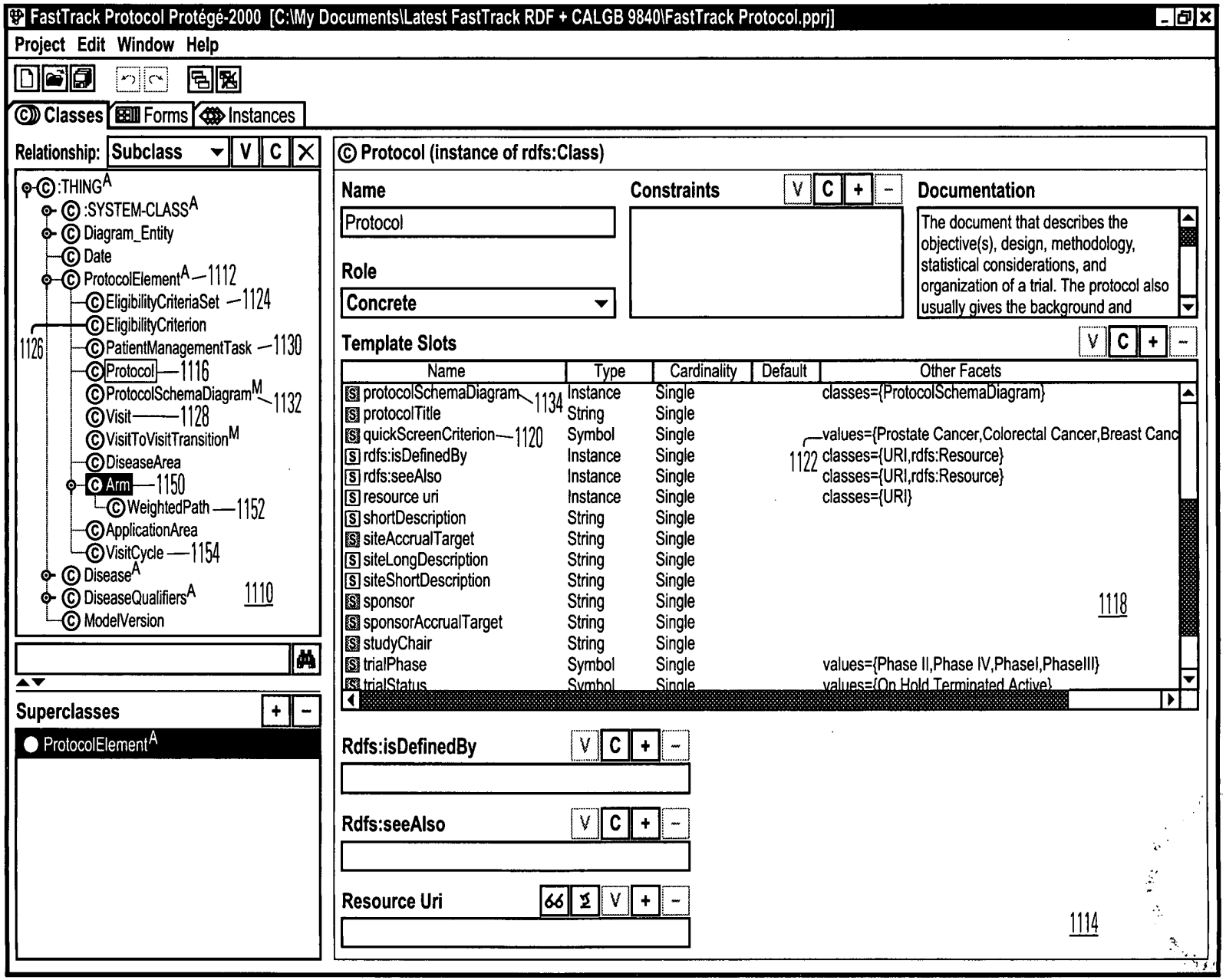

FIG. 11

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

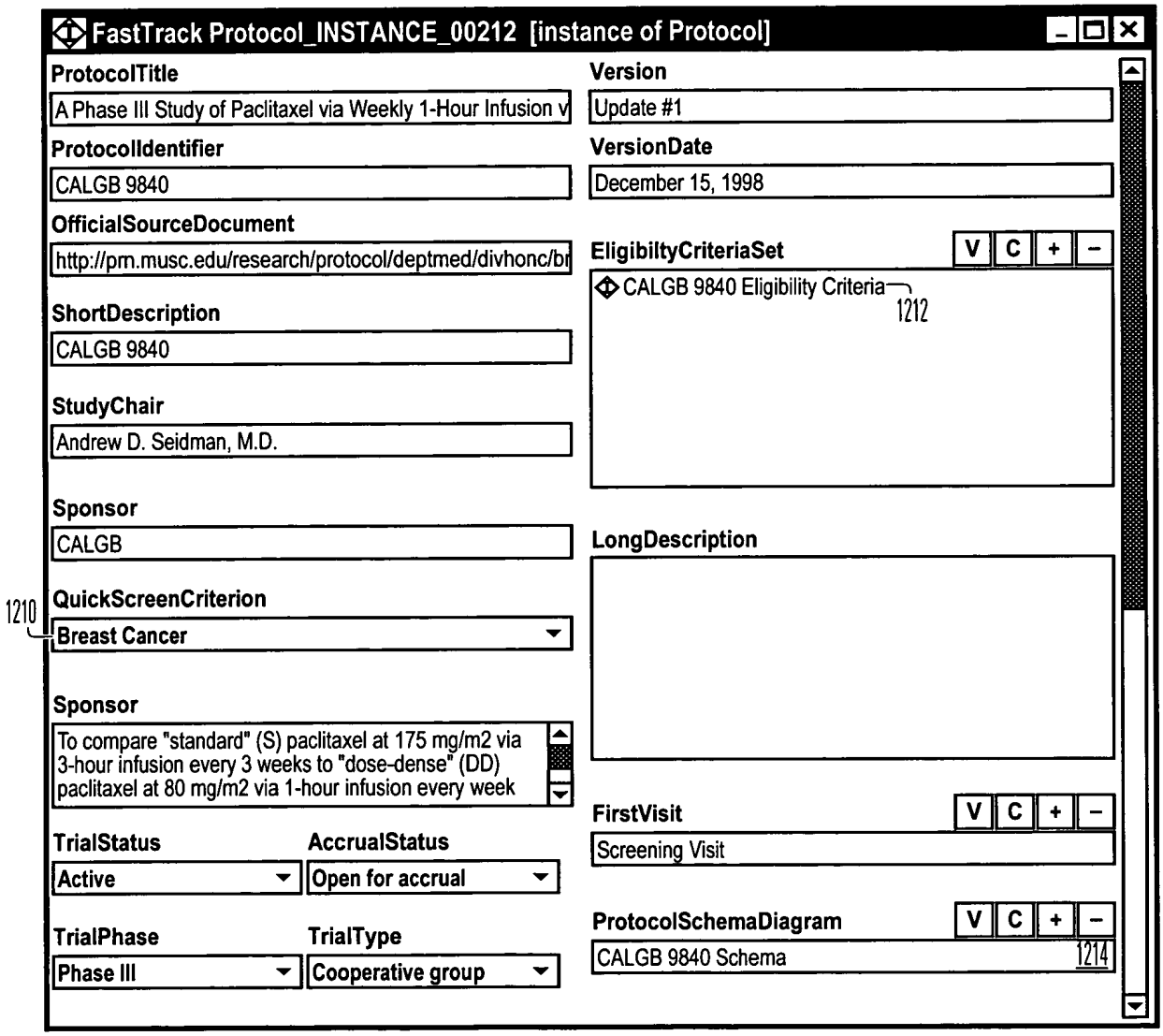
FastTrack Protocol_INSTANCE_00212 [instance of Protocol]
ProtocolTitle
A Phase III Study of Paclitaxel via Weekly 1-Hour Infusion v
ProtocolIdentifier
CALGB 9840
OfficialSourceDocument
http://pm.musc.edu/research/protocol/deptmed/divhonc/br
ShortDescription
CALGB 9840
StudyChair
Andrew D. Seidman, M.D.
Sponsor
CALGB
1210
QuickScreenCriterion
Breast Cancer
Sponsor
To compare "standard" (S) paclitaxel at 175 mg/m2 via 3-hour infusion every 3 weeks to "dose-dense" (DD) paclitaxel at 80 mg/m2 via 1-hour infusion every week
TrialStatus
Active
AccrualStatus
Open for accrual
TrialPhase
Phase III
TrialType
Cooperative group
Version
Update #1
VersionDate
December 15, 1998
EligibiltyCriteriaSet
V C + −
CALGB 9840 Eligibility Criteria
1212
LongDescription
FirstVisit
V C + −
Screening Visit
ProtocolSchemaDiagram
V C + −
CALGB 9840 Schema
1214

FIG. 12

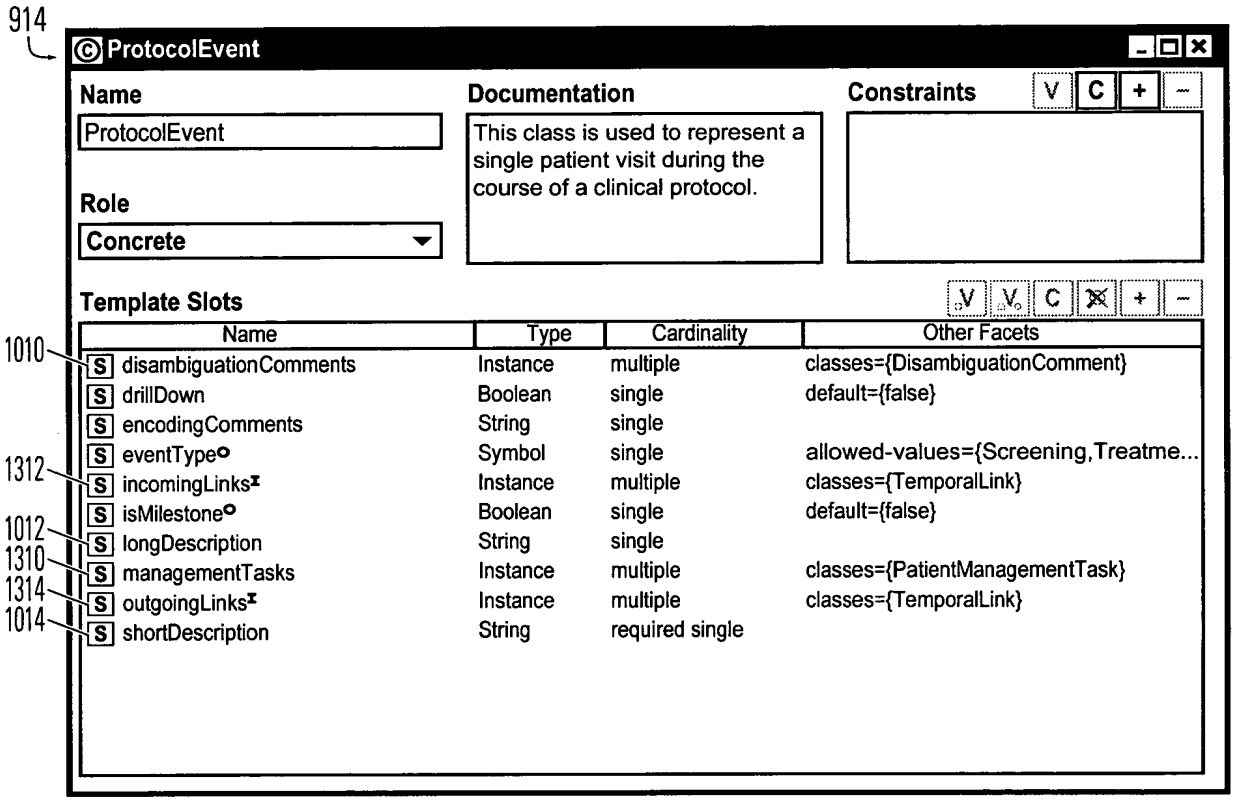
914
ProtocolEvent
Name
ProtocolEvent
Role
Concrete
Documentation
This class is used to represent a single patient visit during the course of a clinical protocol.
Constraints
V
C
+
–
Template Slots
Name
Type
Cardinality
Other Facets
1010
disambiguationComments
Instance
multiple
classes={DisambiguationComment}
drillDown
Boolean
single
default={false}
encodingComments
String
single
1312
eventType
Symbol
single
allowed-values={Screening,Treatme...
incomingLinks
Instance
multiple
classes={TemporalLink}
isMilestone
Boolean
single
default={false}
1012
longDescription
String
single
1310
managementTasks
Instance
multiple
classes={PatientManagementTask}
1314
outgoingLinks
Instance
multiple
classes={TemporalLink}
1014
shortDescription
String
required single

FIG. 13

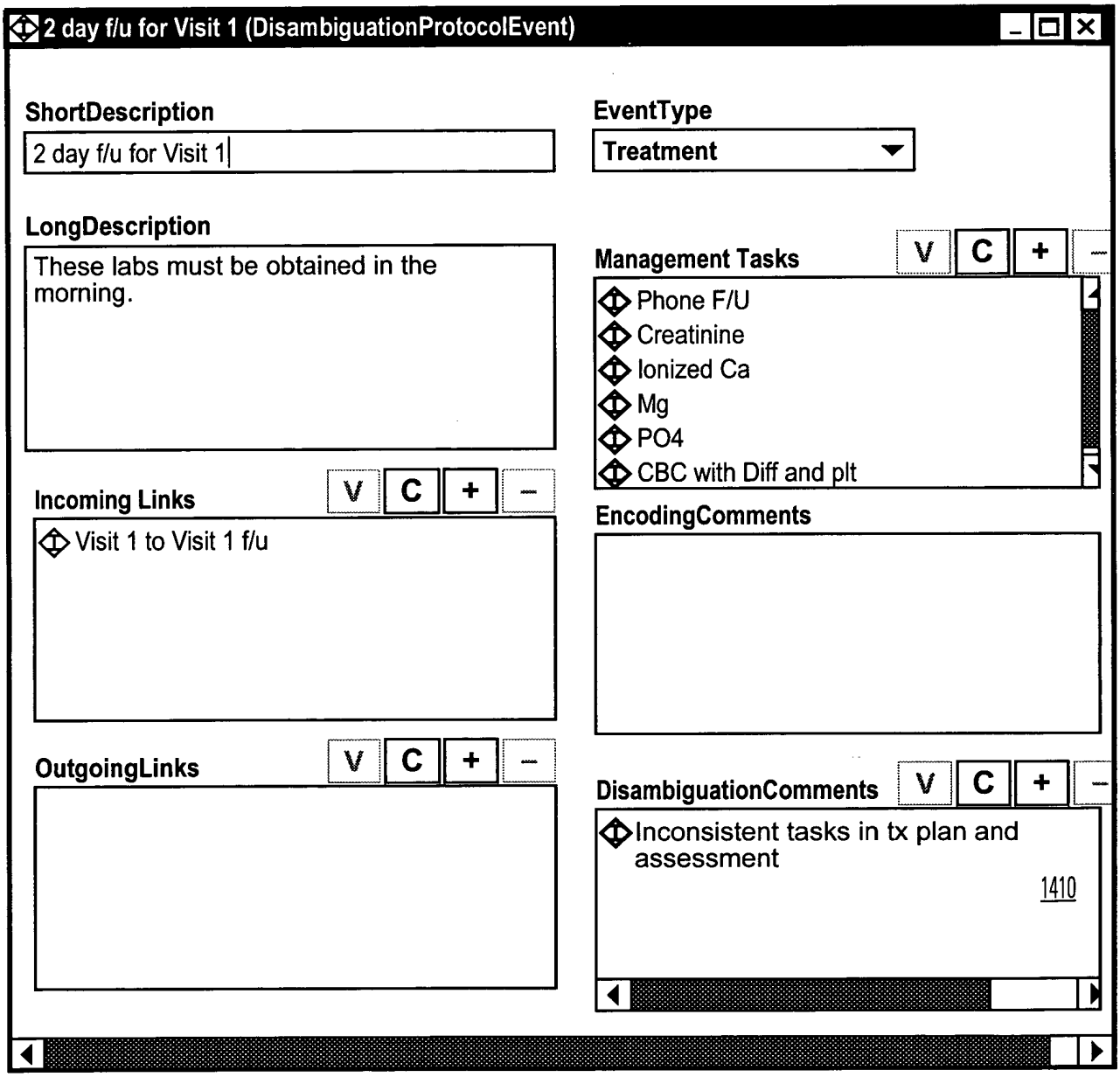

FIG. 14

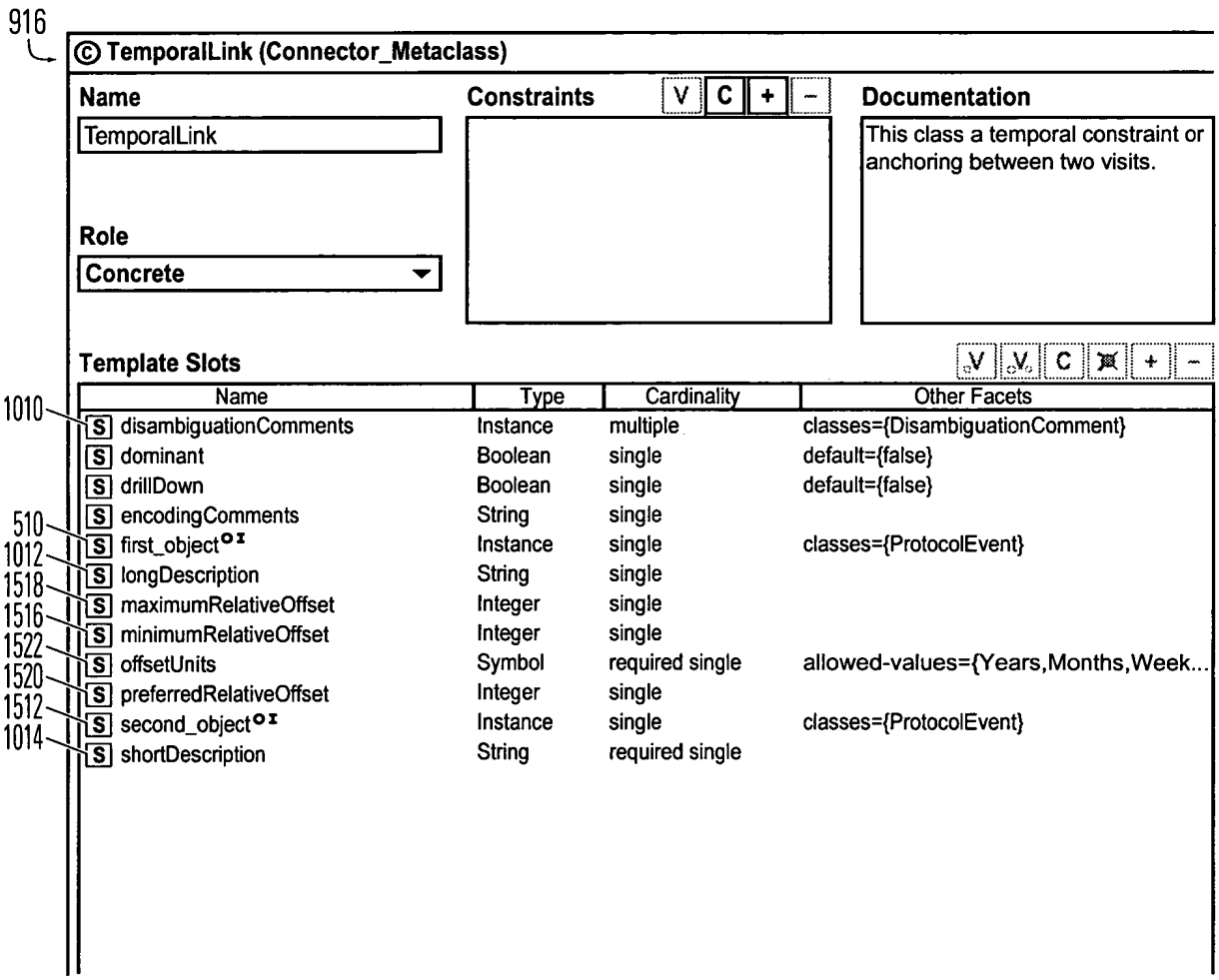
916
© TemporalLink (Connector_Metaclass)
Name
TemporalLink
Role
Concrete
Constraints
V
C
+
–
Documentation
This class a temporal constraint or anchoring between two visits.
Template Slots
Name
Type
Cardinality
Other Facets
1010
S disambiguationComments Instance multiple classes={DisambiguationComment}
S dominant Boolean single default={false}
S drillDown Boolean single default={false}
S encodingComments String single
510
1012
S first_object OI Instance single classes={ProtocolEvent}
1518
S longDescription String single
1516
S maximumRelativeOffset Integer single
1522
S minimumRelativeOffset Integer single
1520
S offsetUnits Symbol required single allowed-values={Years,Months,Week...
1512
S preferredRelativeOffset Integer single
1014
S second_object OI Instance single classes={ProtocolEvent}
S shortDescription String required single

FIG. 15

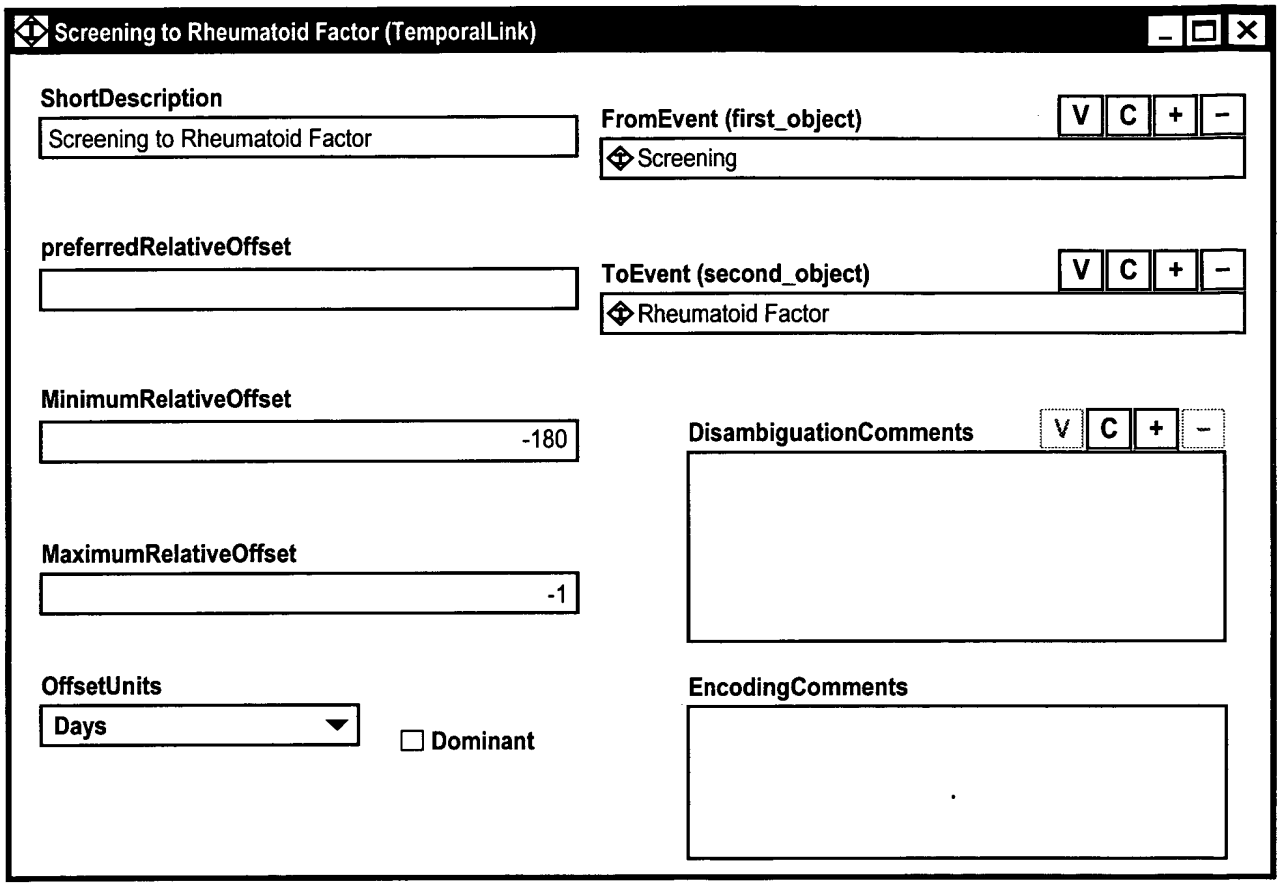
Screening to Rheumatoid Factor (TemporalLink)
ShortDescription
Screening to Rheumatoid Factor
FromEvent (first_object)
V C + -
Screening
preferredRelativeOffset
ToEvent (second_object)
V C + -
Rheumatoid Factor
MinimumRelativeOffset
-180
DisambiguationComments
V C + -
MaximumRelativeOffset
-1
OffsetUnits
Days
Dominant
EncodingComments

FIG. 16

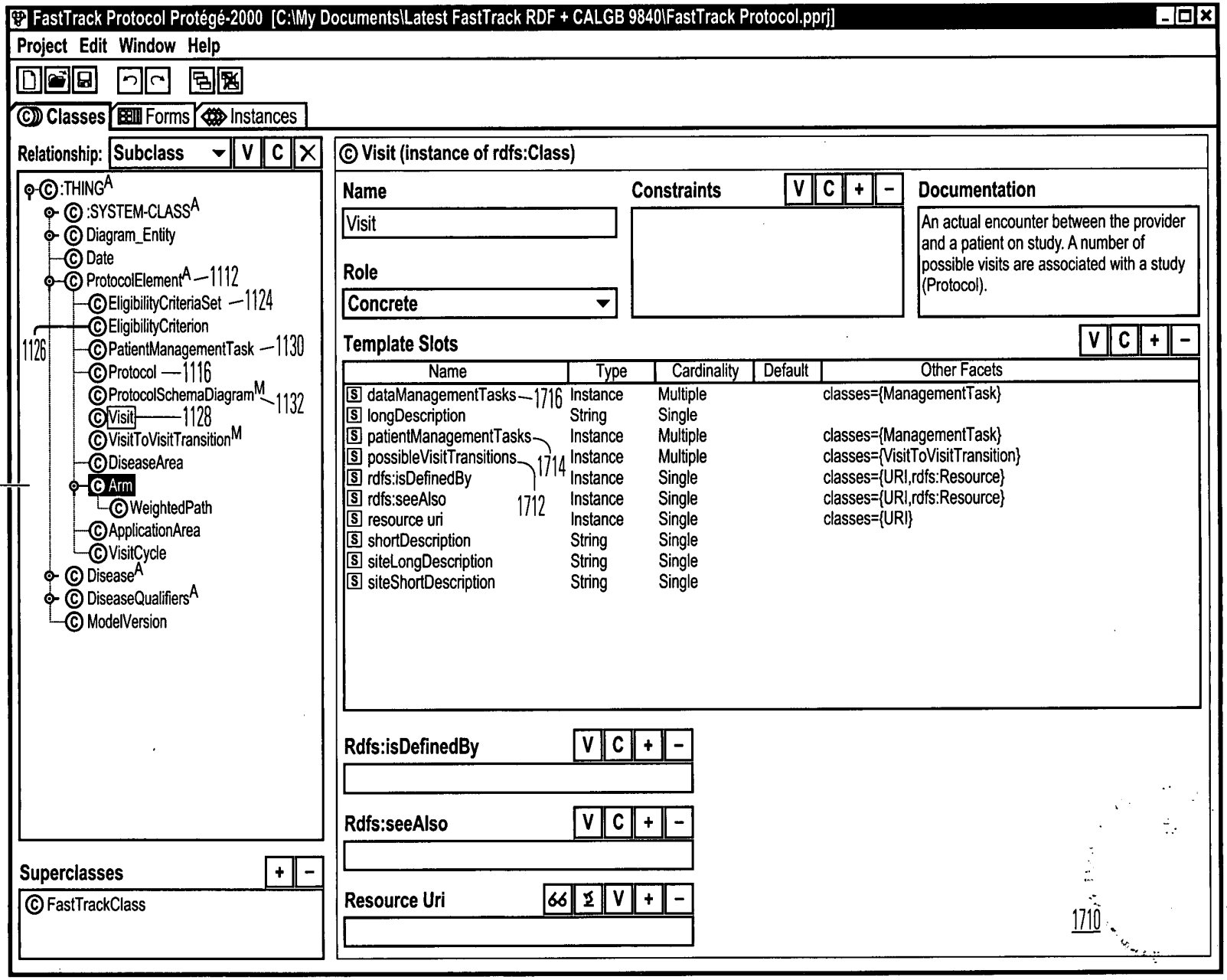

FIG. 17

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

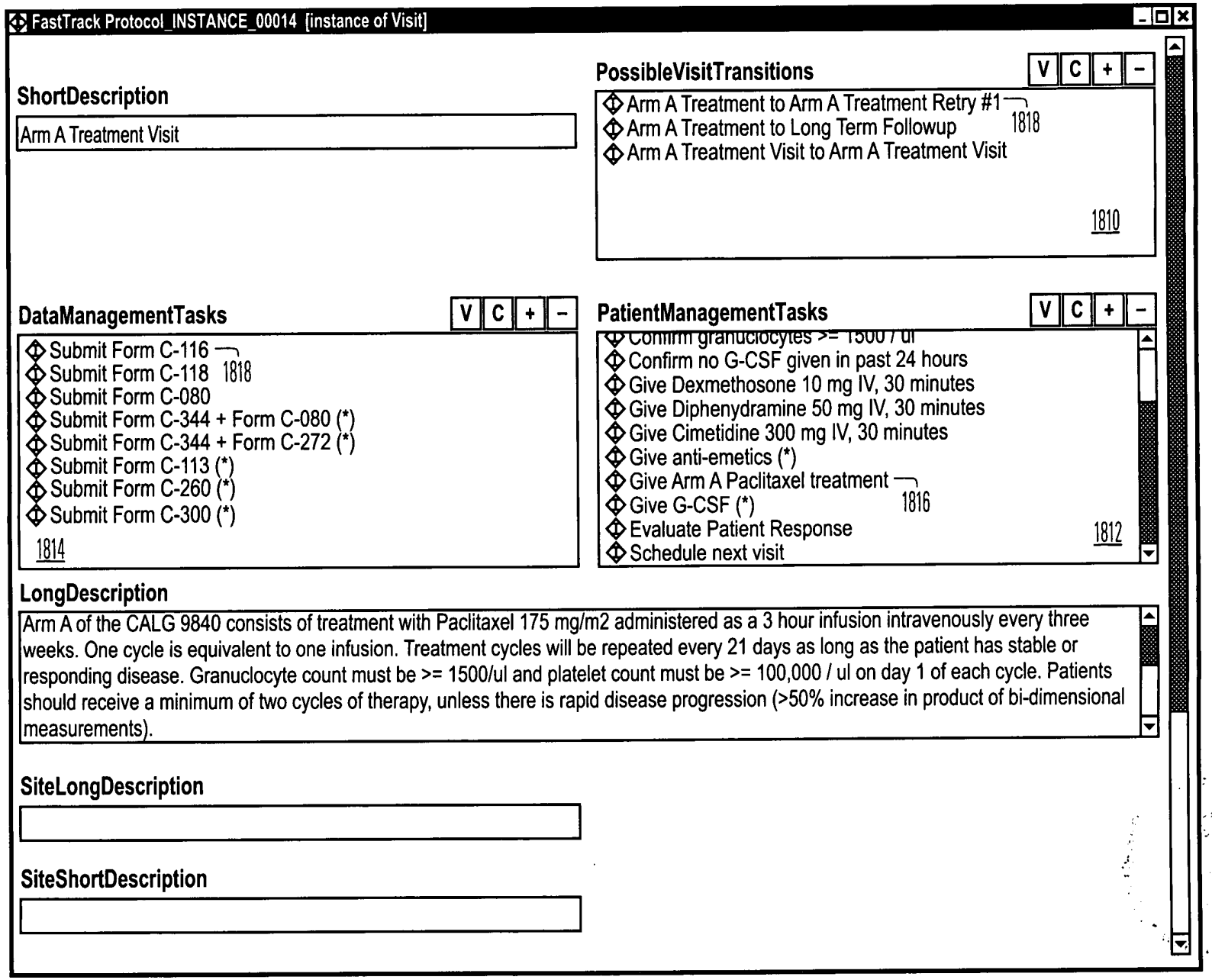

FIG. 18

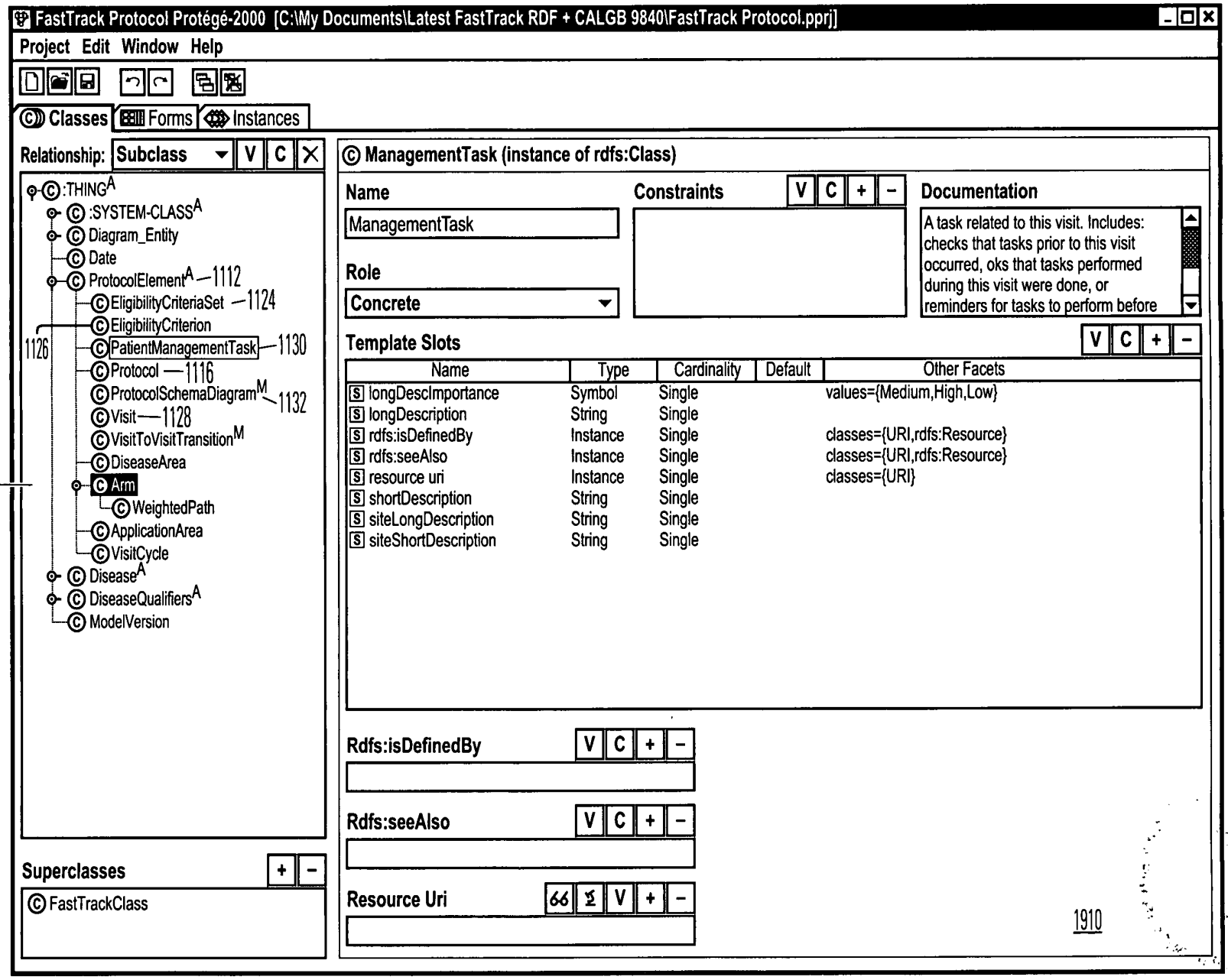

FIG. 19

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

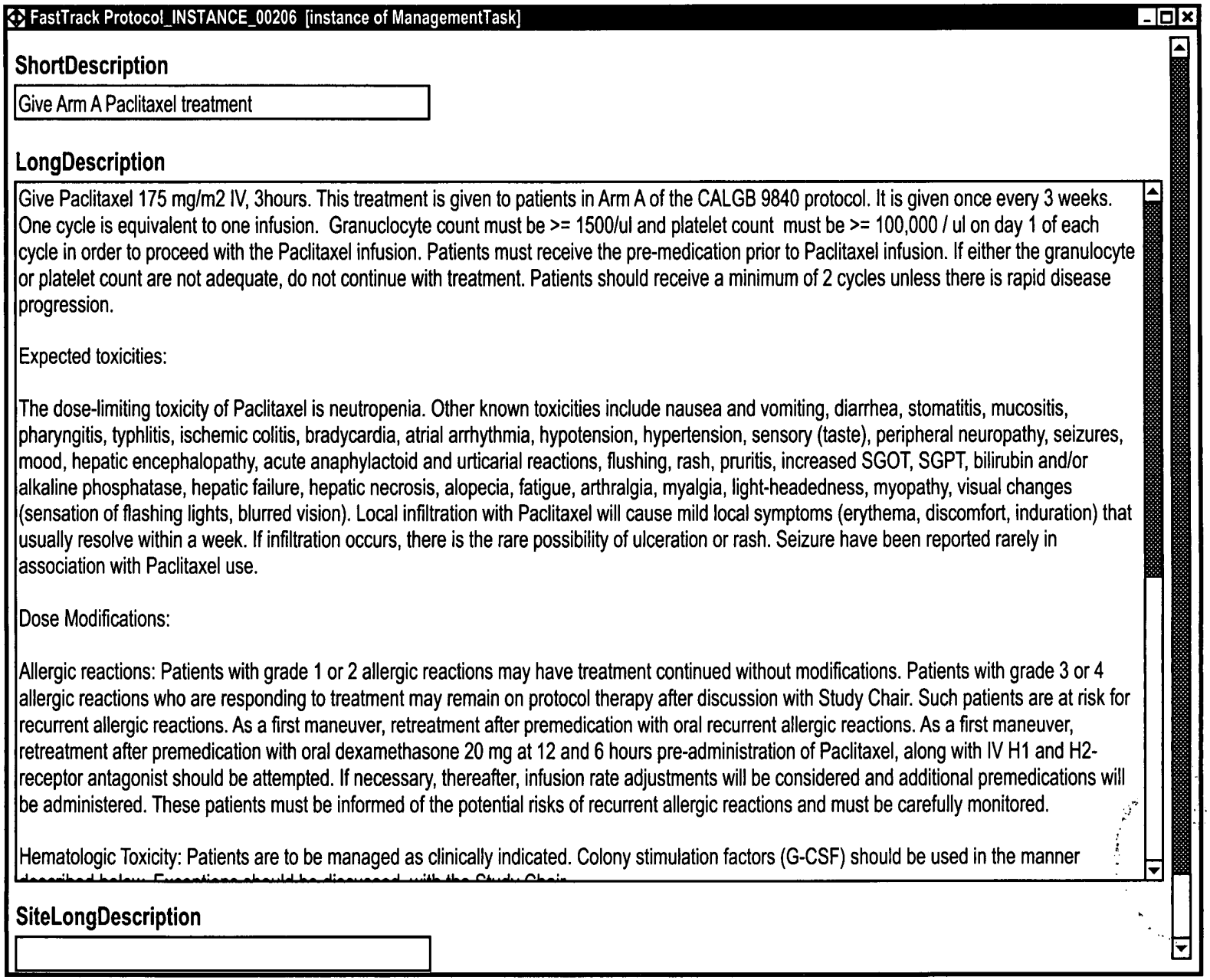
FastTrack Protocol_INSTANCE_00206 [instance of ManagementTask]
ShortDescription
Give Arm A Paclitaxel treatment
LongDescription
Give Paclitaxel 175 mg/m2 IV, 3hours. This treatment is given to patients in Arm A of the CALGB 9840 protocol. It is given once every 3 weeks. One cycle is equivalent to one infusion. Granuclocyte count must be >= 1500/ul and platelet count must be >= 100,000 / ul on day 1 of each cycle in order to proceed with the Paclitaxel infusion. Patients must receive the pre-medication prior to Paclitaxel infusion. If either the granulocyte or platelet count are not adequate, do not continue with treatment. Patients should receive a minimum of 2 cycles unless there is rapid disease progression.
Expected toxicities:
The dose-limiting toxicity of Paclitaxel is neutropenia. Other known toxicities include nausea and vomiting, diarrhea, stomatitis, mucositis, pharyngitis, typhlitis, ischemic colitis, bradycardia, atrial arrhythmia, hypotension, hypertension, sensory (taste), peripheral neuropathy, seizures, mood, hepatic encephalopathy, acute anaphylactoid and urticarial reactions, flushing, rash, pruritis, increased SGOT, SGPT, bilirubin and/or alkaline phosphatase, hepatic failure, hepatic necrosis, alopecia, fatigue, arthralgia, myalgia, light-headedness, myopathy, visual changes (sensation of flashing lights, blurred vision). Local infiltration with Paclitaxel will cause mild local symptoms (erythema, discomfort, induration) that usually resolve within a week. If infiltration occurs, there is the rare possibility of ulceration or rash. Seizure have been reported rarely in association with Paclitaxel use.
Dose Modifications:
Allergic reactions: Patients with grade 1 or 2 allergic reactions may have treatment continued without modifications. Patients with grade 3 or 4 allergic reactions who are responding to treatment may remain on protocol therapy after discussion with Study Chair. Such patients are at risk for recurrent allergic reactions. As a first maneuver, retreatment after premedication with oral recurrent allergic reactions. As a first maneuver, retreatment after premedication with oral dexamethasone 20 mg at 12 and 6 hours pre-administration of Paclitaxel, along with IV H1 and H2-receptor antagonist should be attempted. If necessary, thereafter, infusion rate adjustments will be considered and additional premedications will be administered. These patients must be informed of the potential risks of recurrent allergic reactions and must be carefully monitored.
Hematologic Toxicity: Patients are to be managed as clinically indicated. Colony stimulation factors (G-CSF) should be used in the manner
SiteLongDescription

FIG. 20

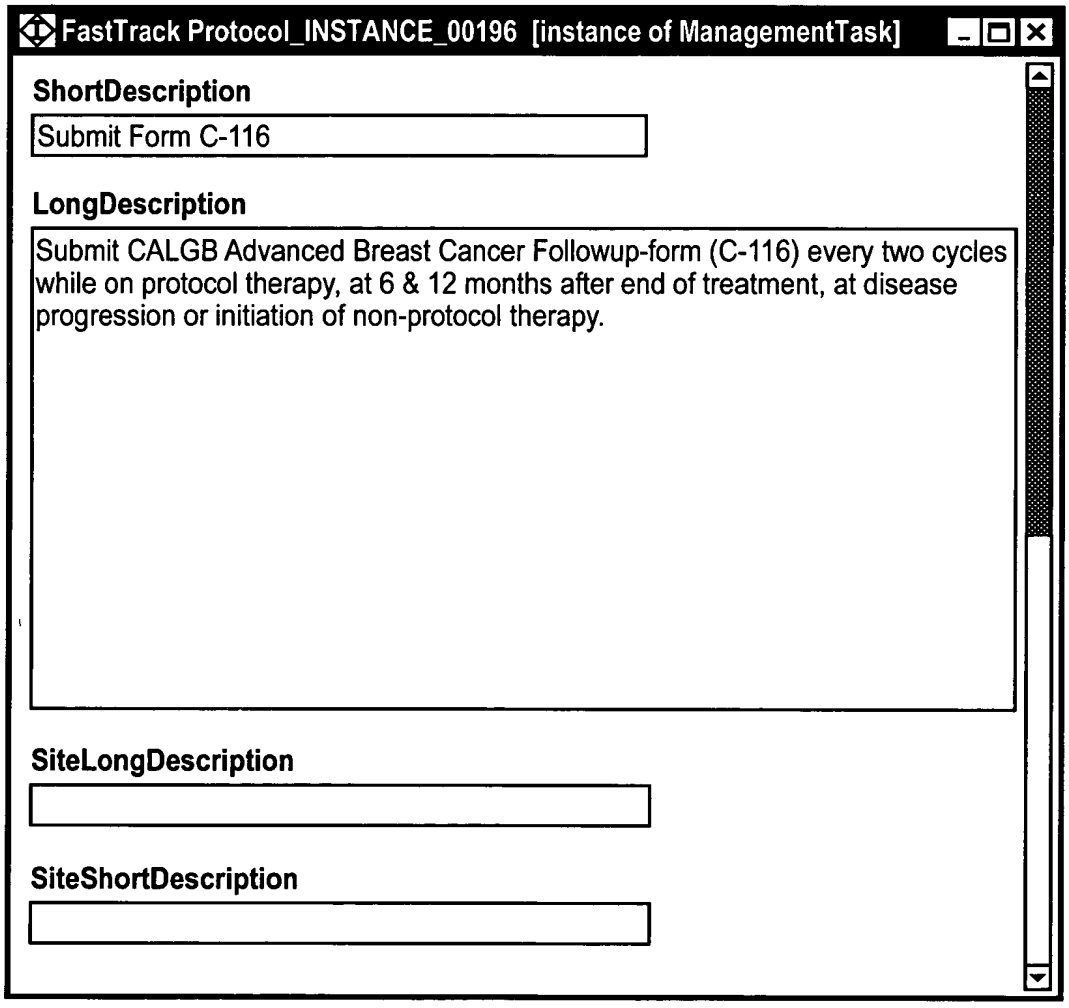

FIG. 21

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

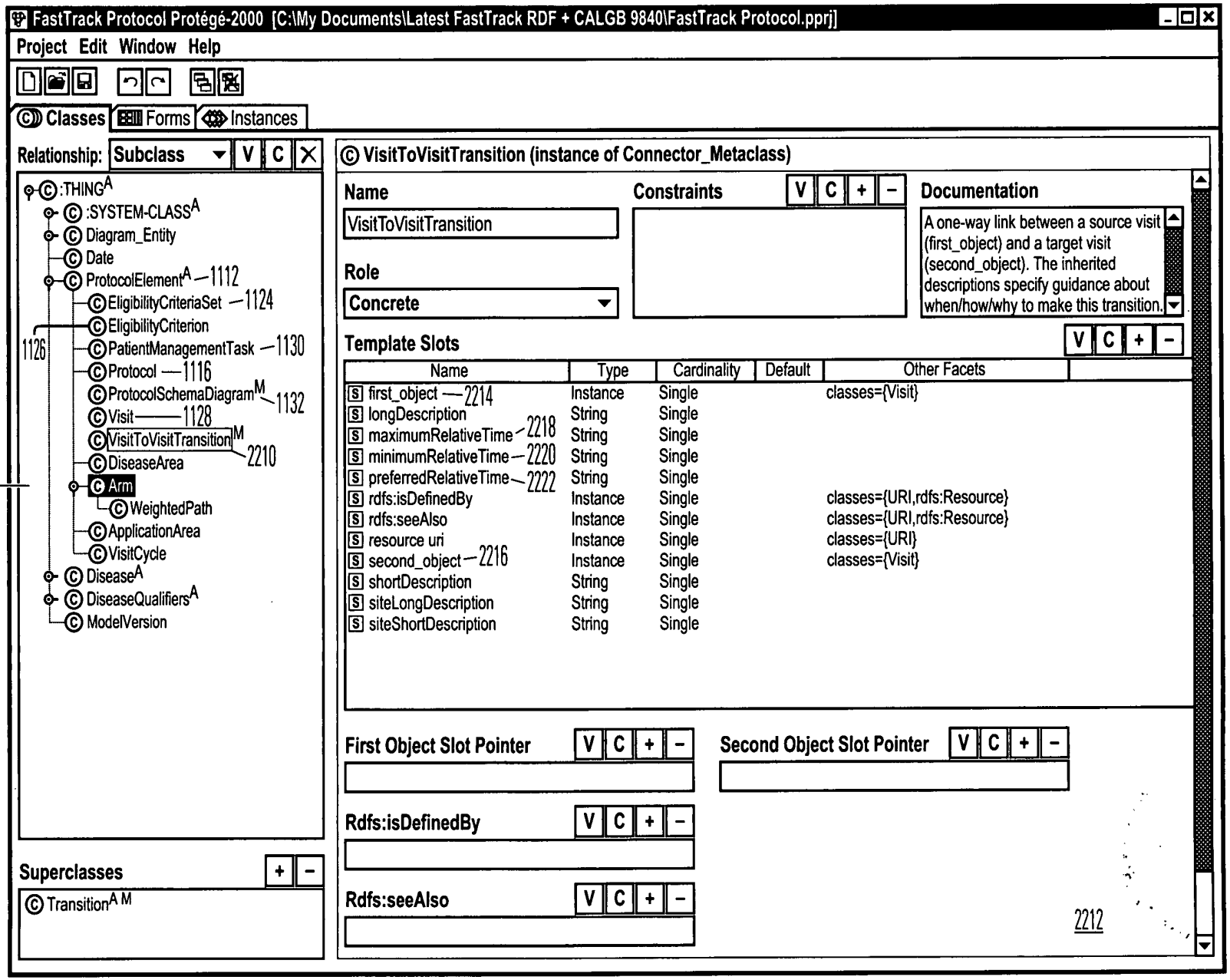

FIG. 22

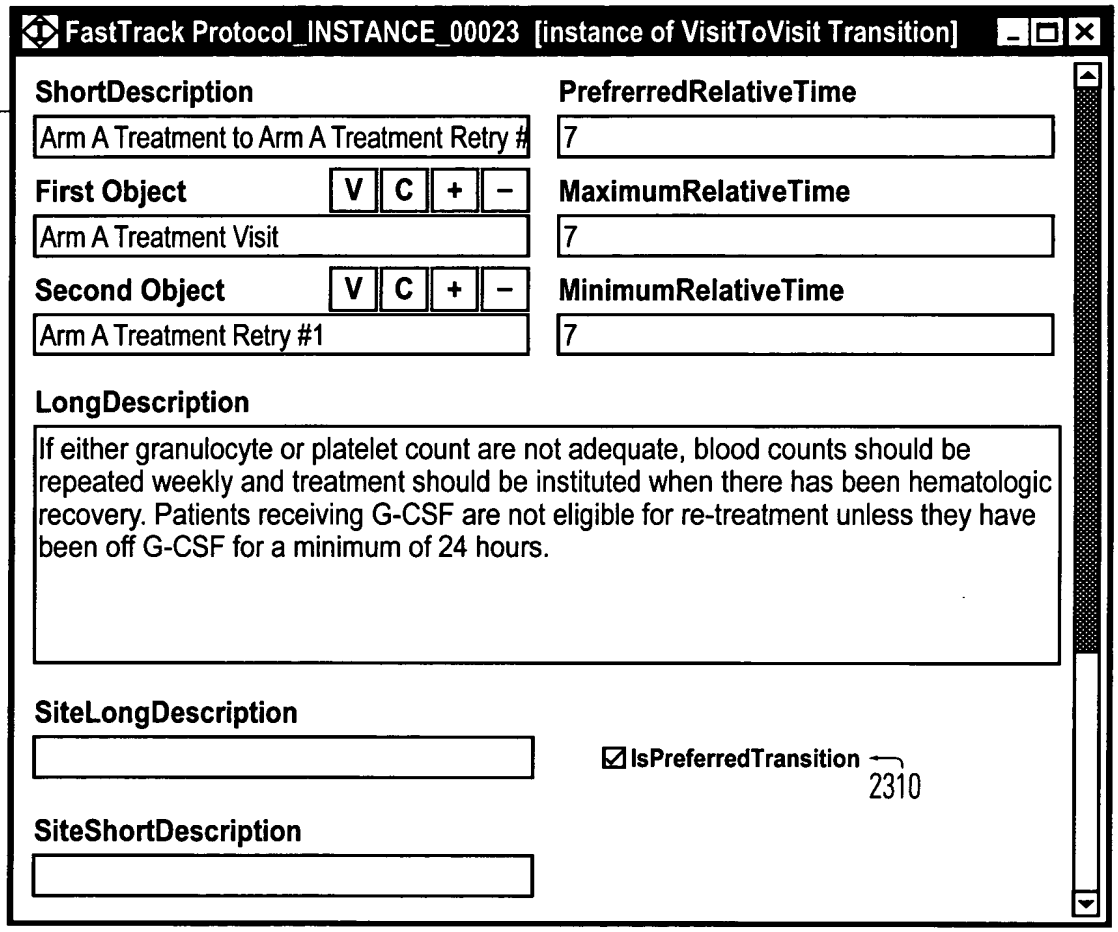
FastTrack Protocol_INSTANCE_00023 [instance of VisitToVisit Transition]
1818
ShortDescription
Arm A Treatment to Arm A Treatment Retry #
PrefrerredRelativeTime
7
First Object
V
C
+
–
Arm A Treatment Visit
MaximumRelativeTime
7
Second Object
V
C
+
–
Arm A Treatment Retry #1
MinimumRelativeTime
7
LongDescription
If either granulocyte or platelet count are not adequate, blood counts should be repeated weekly and treatment should be instituted when there has been hematologic recovery. Patients receiving G-CSF are not eligible for re-treatment unless they have been off G-CSF for a minimum of 24 hours.
SiteLongDescription
IsPreferredTransition
2310
SiteShortDescription

FIG. 23

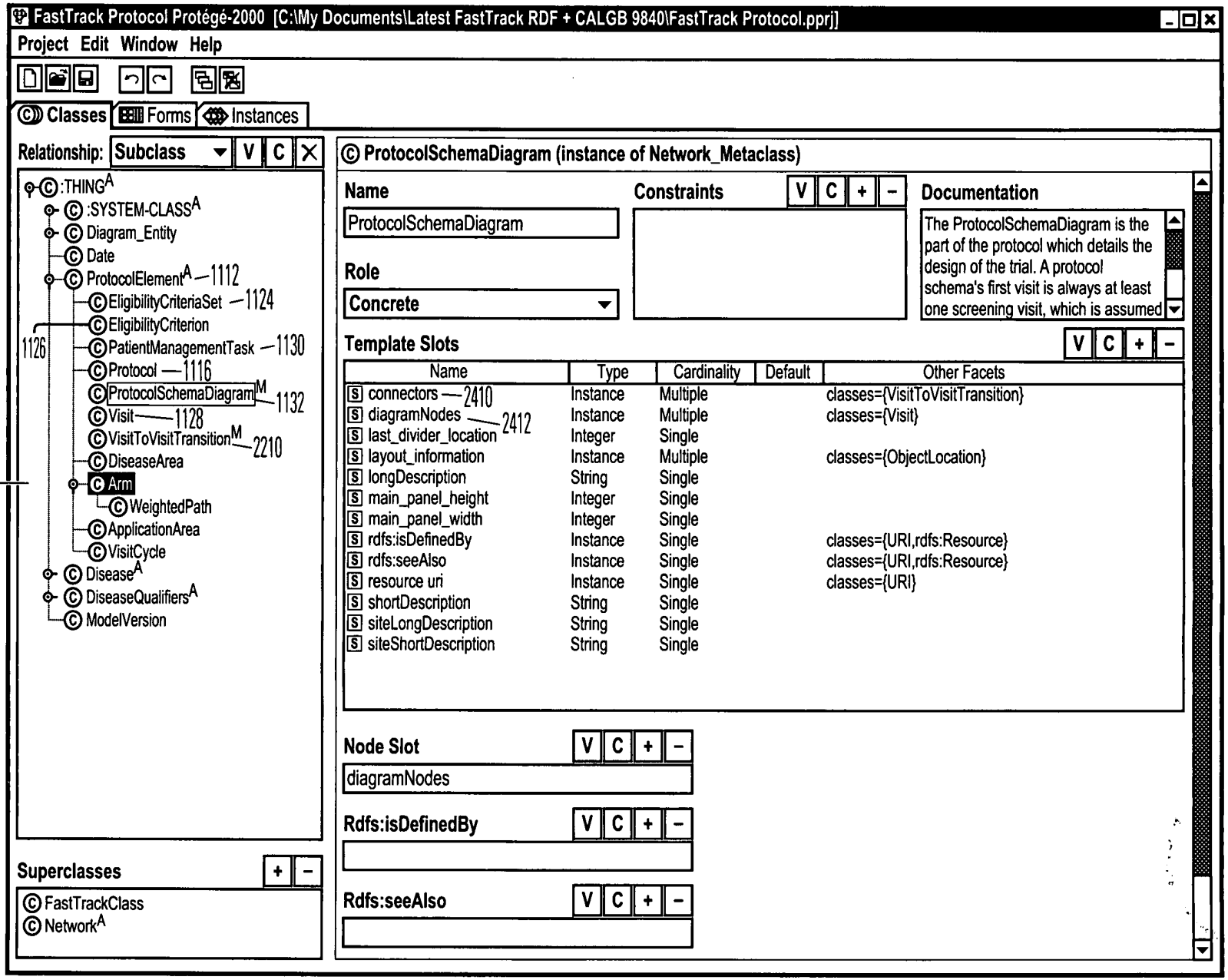

FIG. 24

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

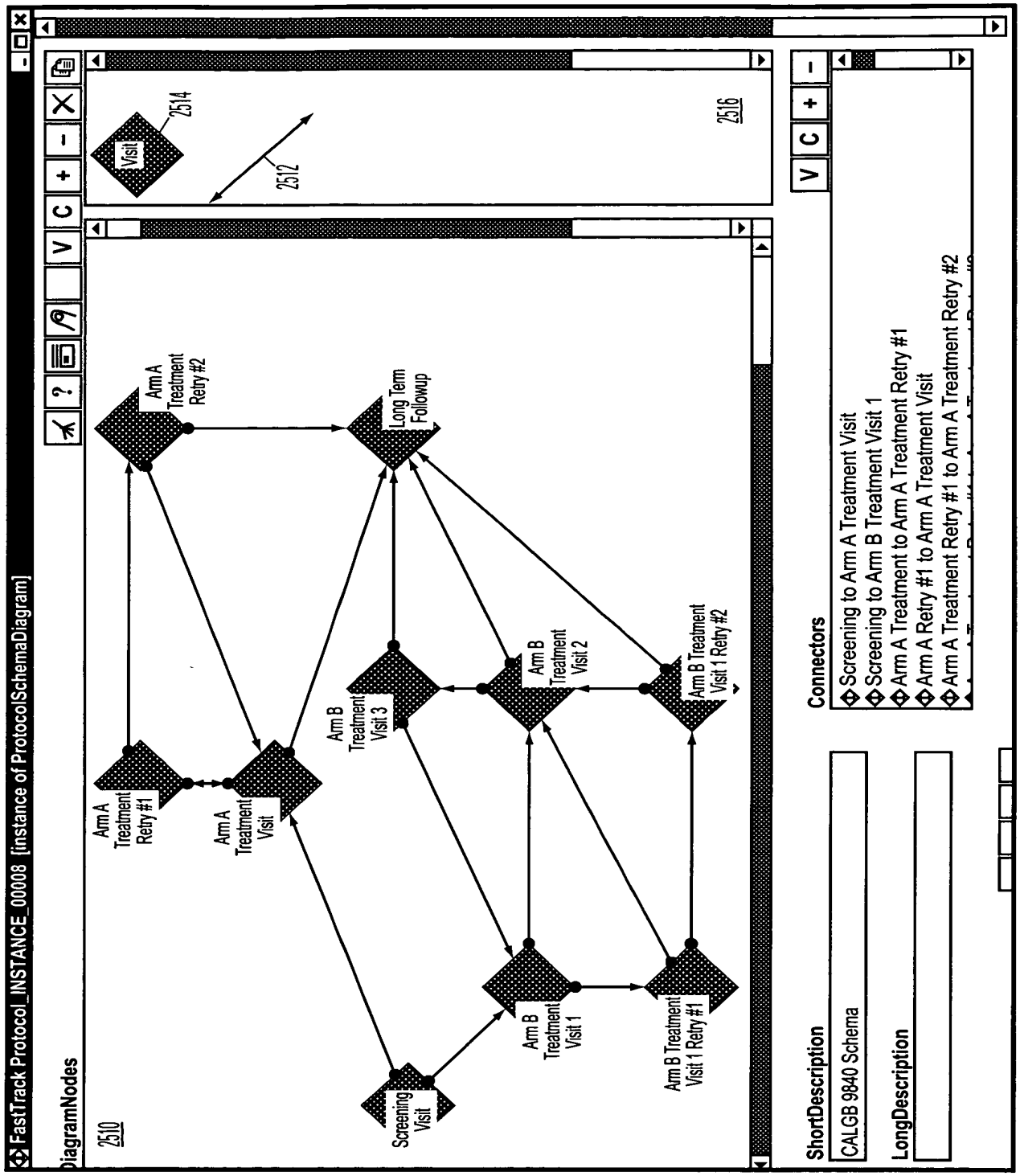
FastTrack Protocol_INSTANCE_00008 [instance of ProtocolSchemaDiagram]
DiagramNodes
2510
Arm A Treatment Retry #2
Long Term Followup
Arm A Treatment Retry #1
Arm A Treatment Visit
Arm B Treatment Visit 3
Arm B Treatment Visit 2
Arm B Treatment Visit 1 Retry #2
Screening Visit
Arm B Treatment Visit 1
Arm B Treatment Visit 1 Retry #1
2512
2514
Visit
2516
Connectors
Screening to Arm A Treatment Visit
Screening to Arm B Treatment Visit 1
Arm A Treatment to Arm A Treatment Retry #1
Arm A Retry #1 to Arm A Treatment Visit
Arm A Treatment Retry #1 to Arm A Treatment Retry #2
ShortDescription
CALGB 9840 Schema
LongDescription

FIG. 25

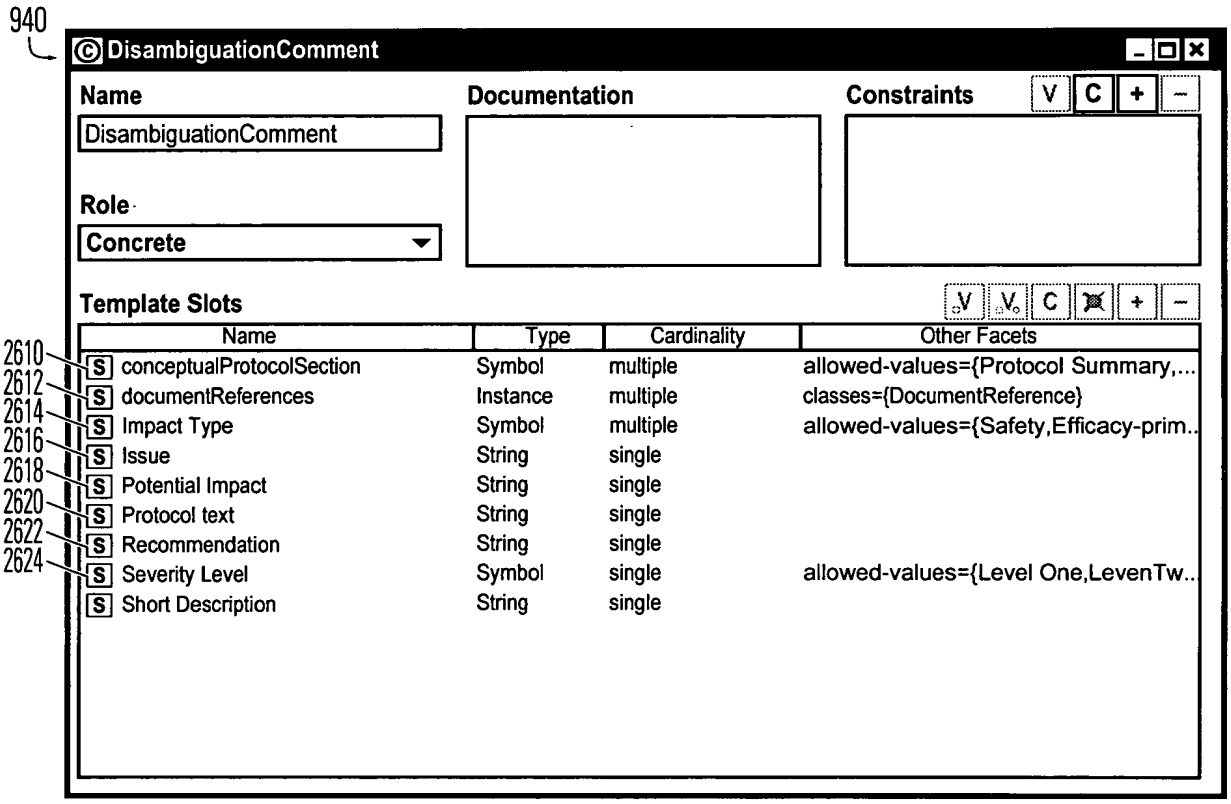
940
DisambiguationComment
Name
DisambiguationComment
Documentation
Constraints
V
C
+
–
Role
Concrete
Template Slots
Name
Type
Cardinality
Other Facets
2610
conceptualProtocolSection
Symbol
multiple
allowed-values={Protocol Summary,...
2612
documentReferences
Instance
multiple
classes={DocumentReference}
2614
Impact Type
Symbol
multiple
allowed-values={Safety,Efficacy-prim..
2616
Issue
String
single
2618
Potential Impact
String
single
2620
Protocol text
String
single
2622
Recommendation
String
single
2624
Severity Level
Symbol
single
allowed-values={Level One,LevenTw..
Short Description
String
single

FIG. 26

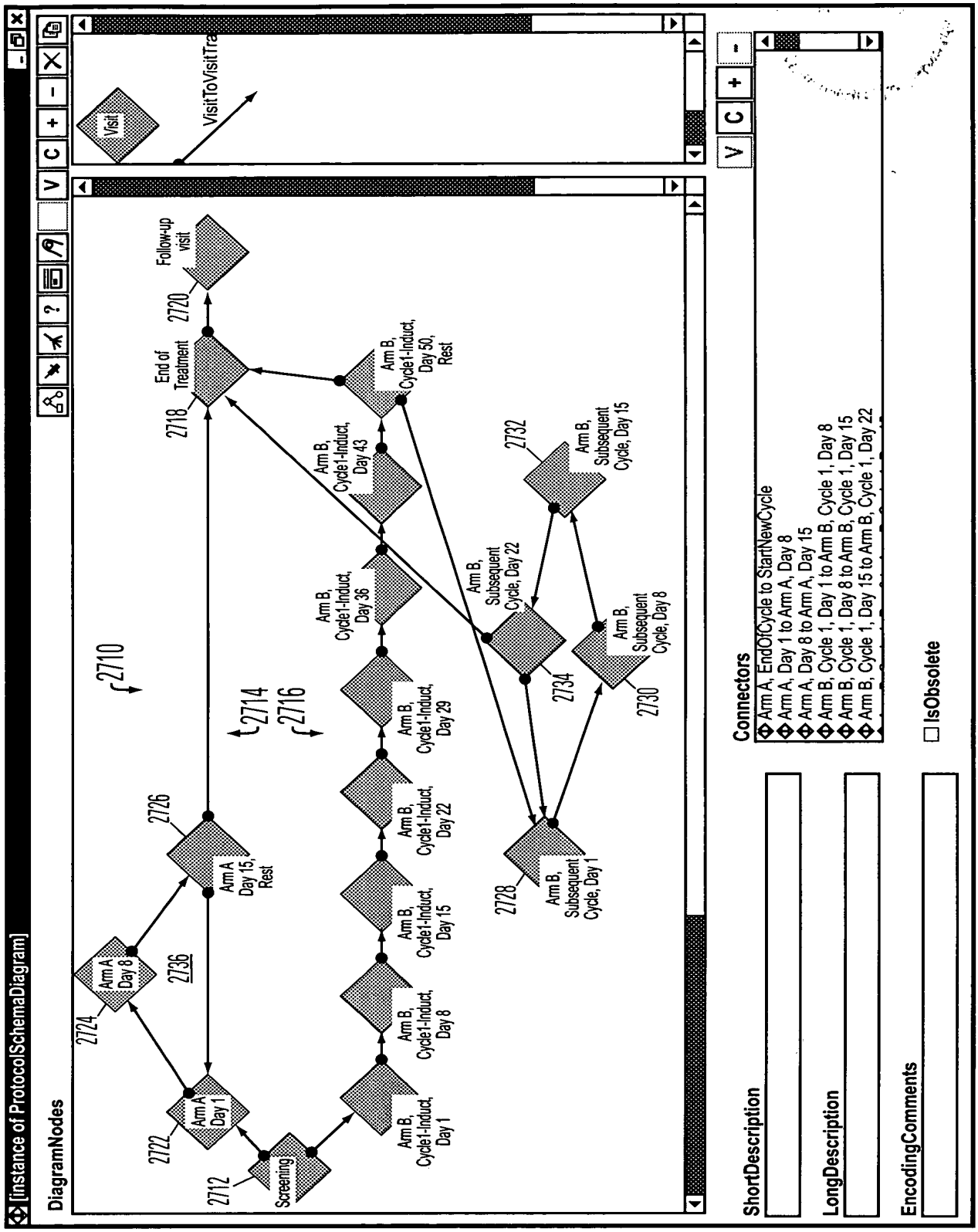
[instance of ProtocolSchemaDiagram]
DiagramNodes
Visit
VisitToVisitTra
2710
2712
Screening
2714
2716
2718
End of Treatment
2720
Follow-up visit
2722
Arm A Day 1
2724
Arm A Day 8
2726
Arm A Day 15, Rest
2728
Arm B, Subsequent Cycle, Day 1
2730
Arm B, Subsequent Cycle, Day 8
2732
Arm B, Subsequent Cycle, Day 15
2734
Arm B, Subsequent Cycle, Day 22
2736
Arm B, Cycle1-Induct, Day 1
Arm B, Cycle1-Induct, Day 8
Arm B, Cycle1-Induct, Day 15
Arm B, Cycle1-Induct, Day 22
Arm B, Cycle1-Induct, Day 29
Arm B, Cycle1-Induct, Day 36
Arm B, Cycle1-Induct, Day 43
Arm B, Cycle1-Induct, Day 50, Rest
Connectors
Arm A, EndOfCycle to StartNewCycle
Arm A, Day 1 to Arm A, Day 8
Arm A, Day 8 to Arm A, Day 15
Arm B, Cycle 1, Day 1 to Arm B, Cycle 1, Day 8
Arm B, Cycle 1, Day 8 to Arm B, Cycle 1, Day 15
Arm B, Cycle 1, Day 15 to Arm B, Cycle 1, Day 22
ShortDescription
LongDescription
EncodingComments
IsObsolete

FIG. 27

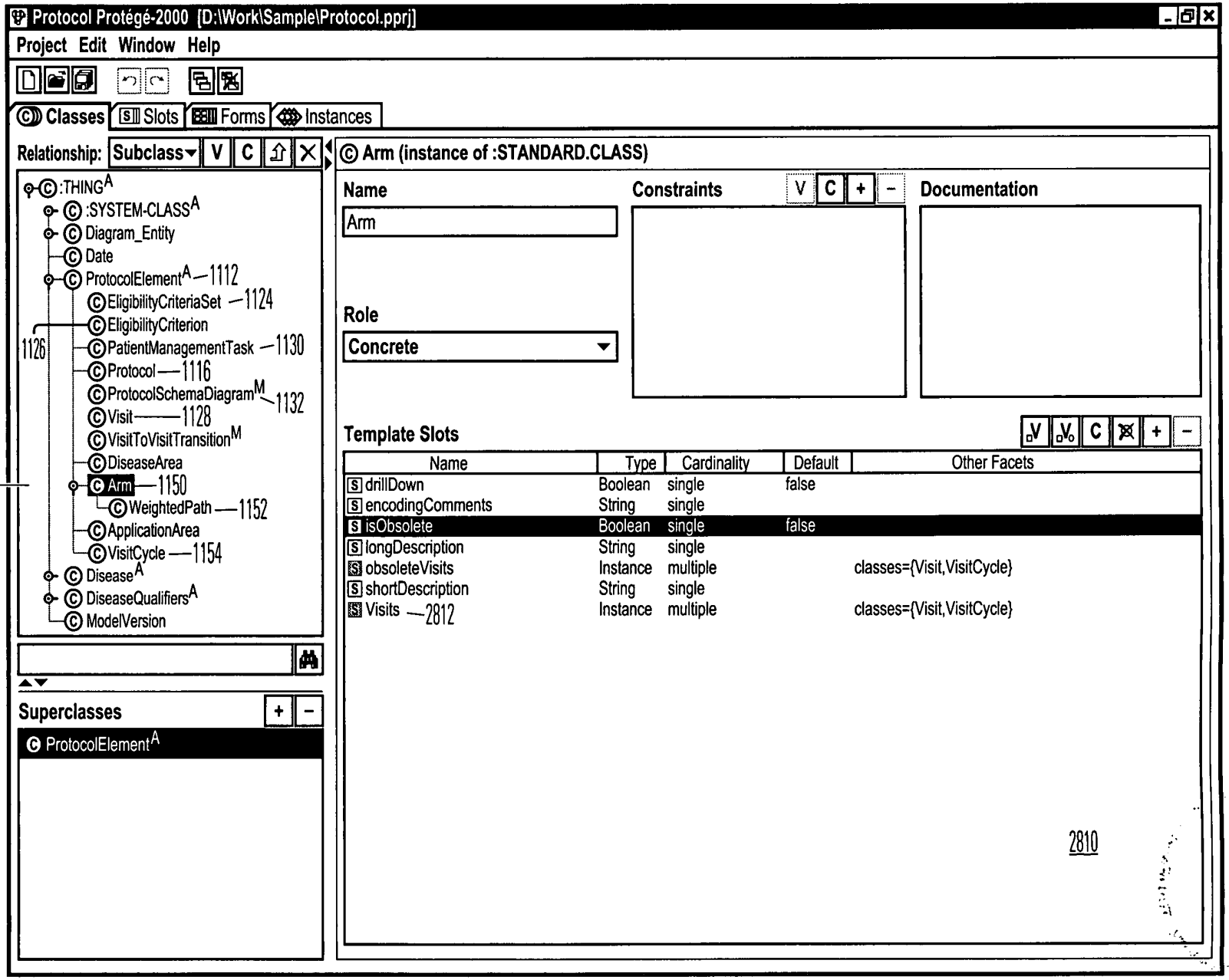

FIG. 28

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

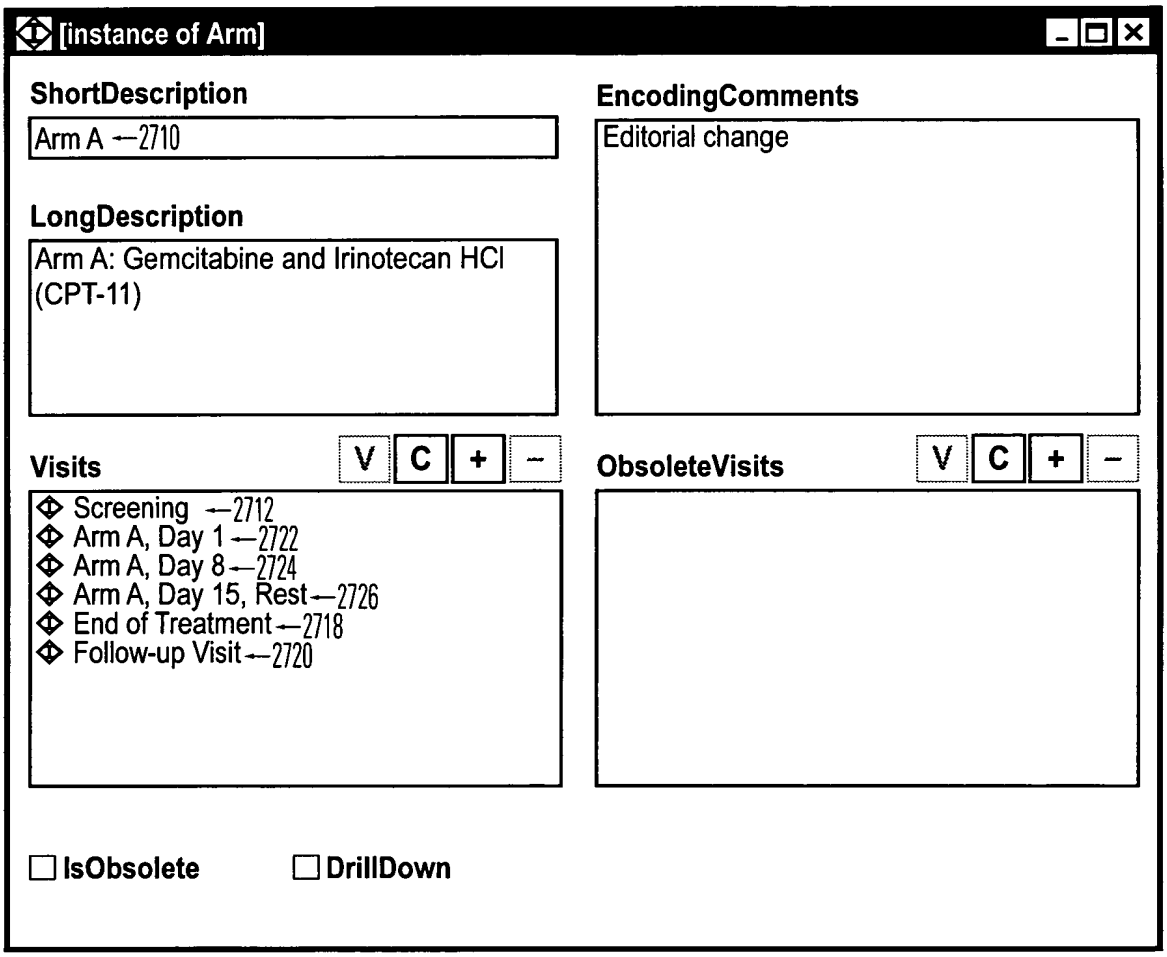

FIG. 29

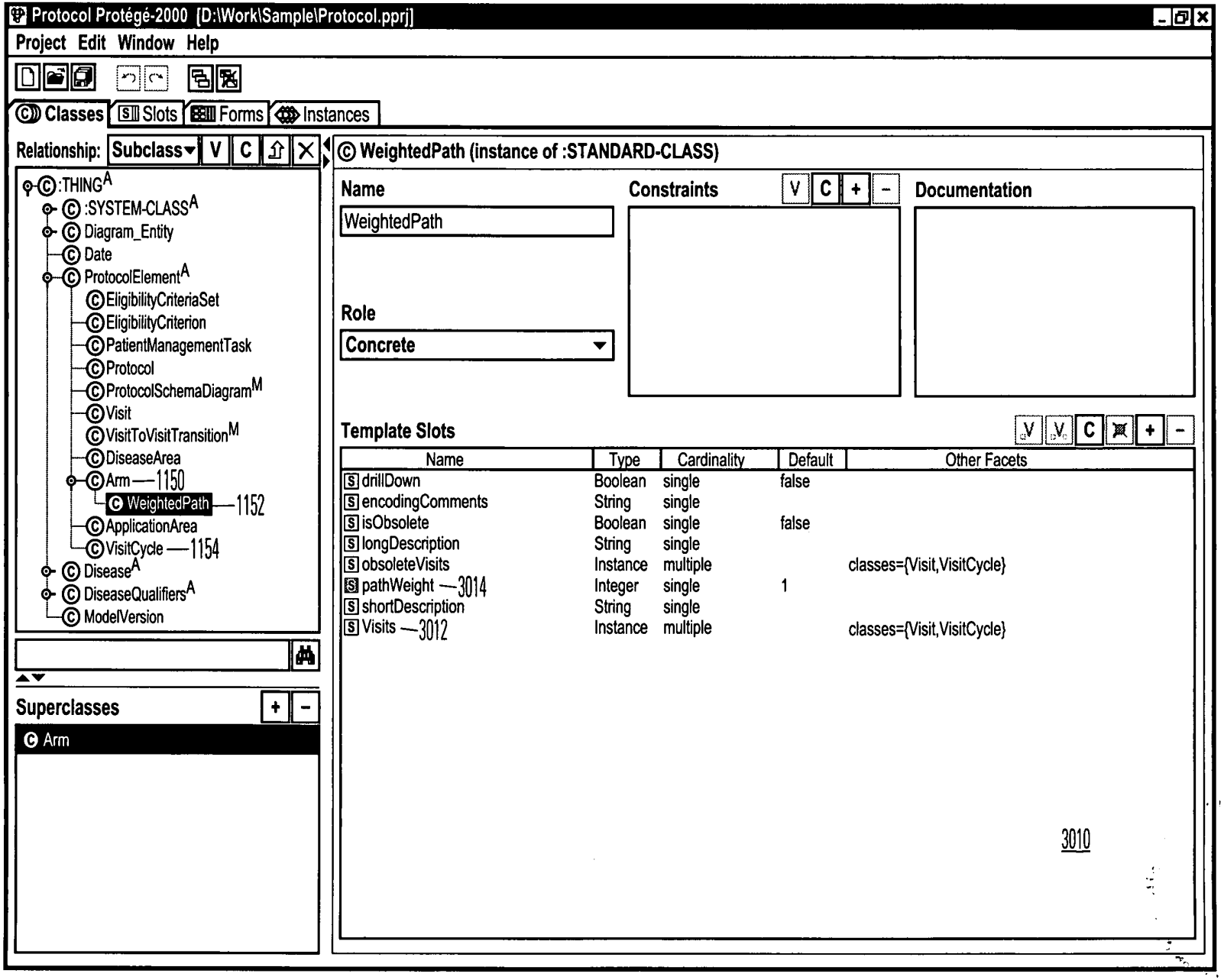

FIG. 30

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

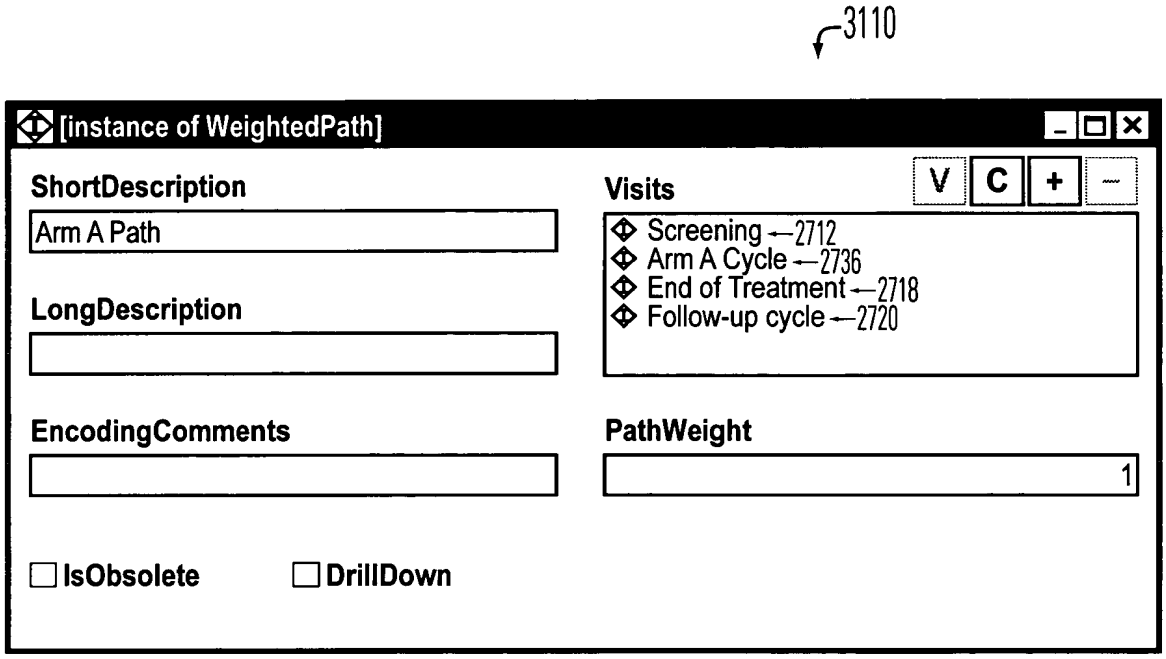

FIG. 31

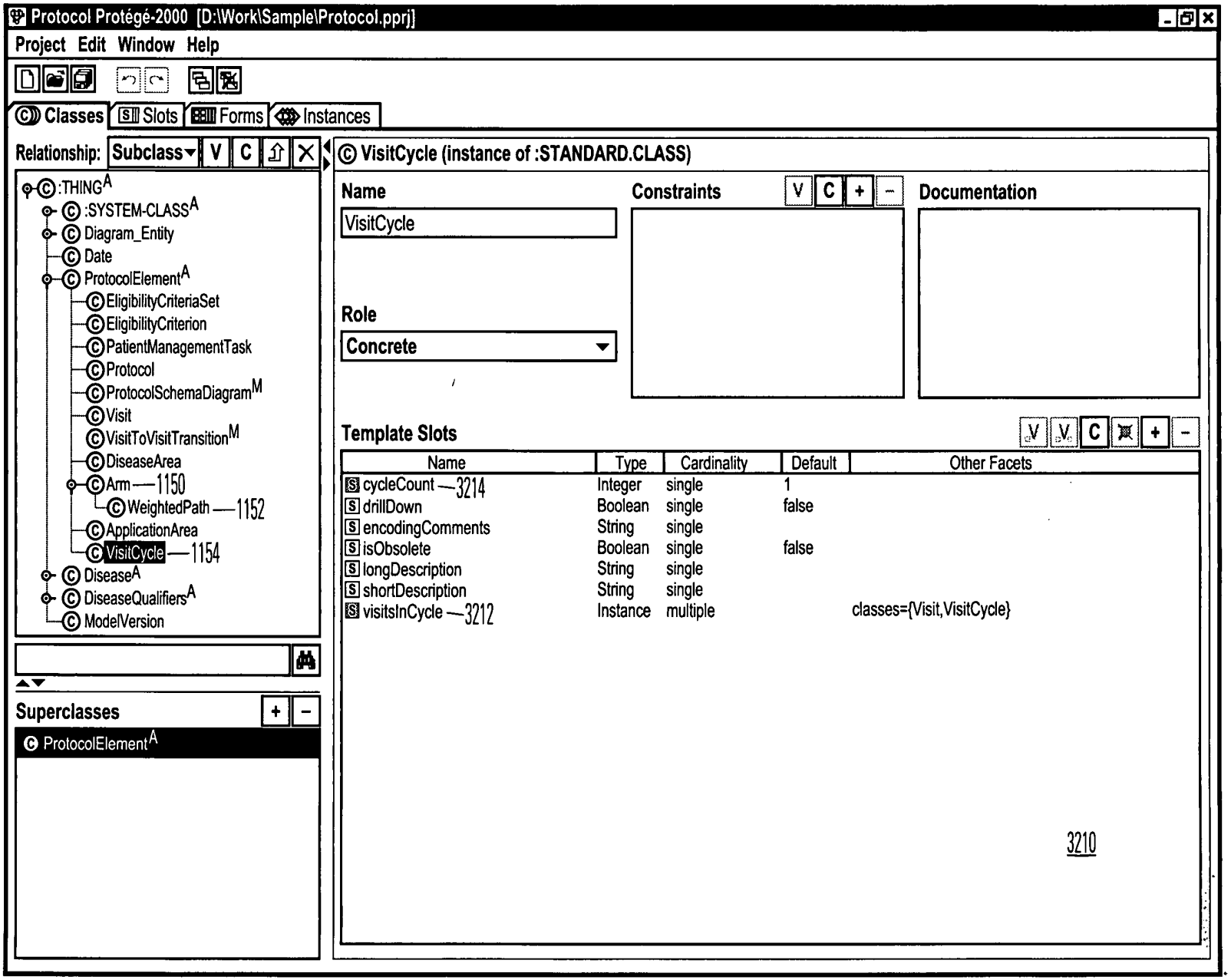

FIG. 32

Inventors: Michael G. Kahn et al.
Title: Protocol Disambiguation Using a Model-Based Methodology (as amended)
Application No. 09/974,781

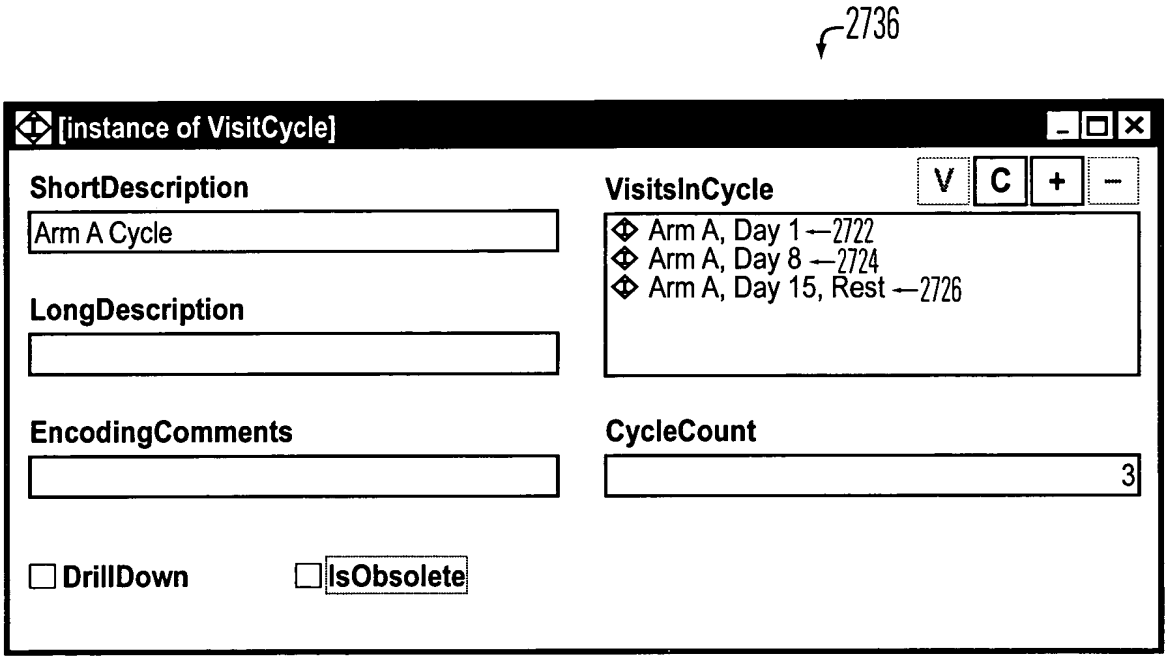
2736
[instance of VisitCycle]
ShortDescription
Arm A Cycle
LongDescription
EncodingComments
VisitsInCycle
V
C
+
–
Arm A, Day 1 —2722
Arm A, Day 8 —2724
Arm A, Day 15, Rest —2726
CycleCount
3
DrillDown
IsObsolete

FIG. 33

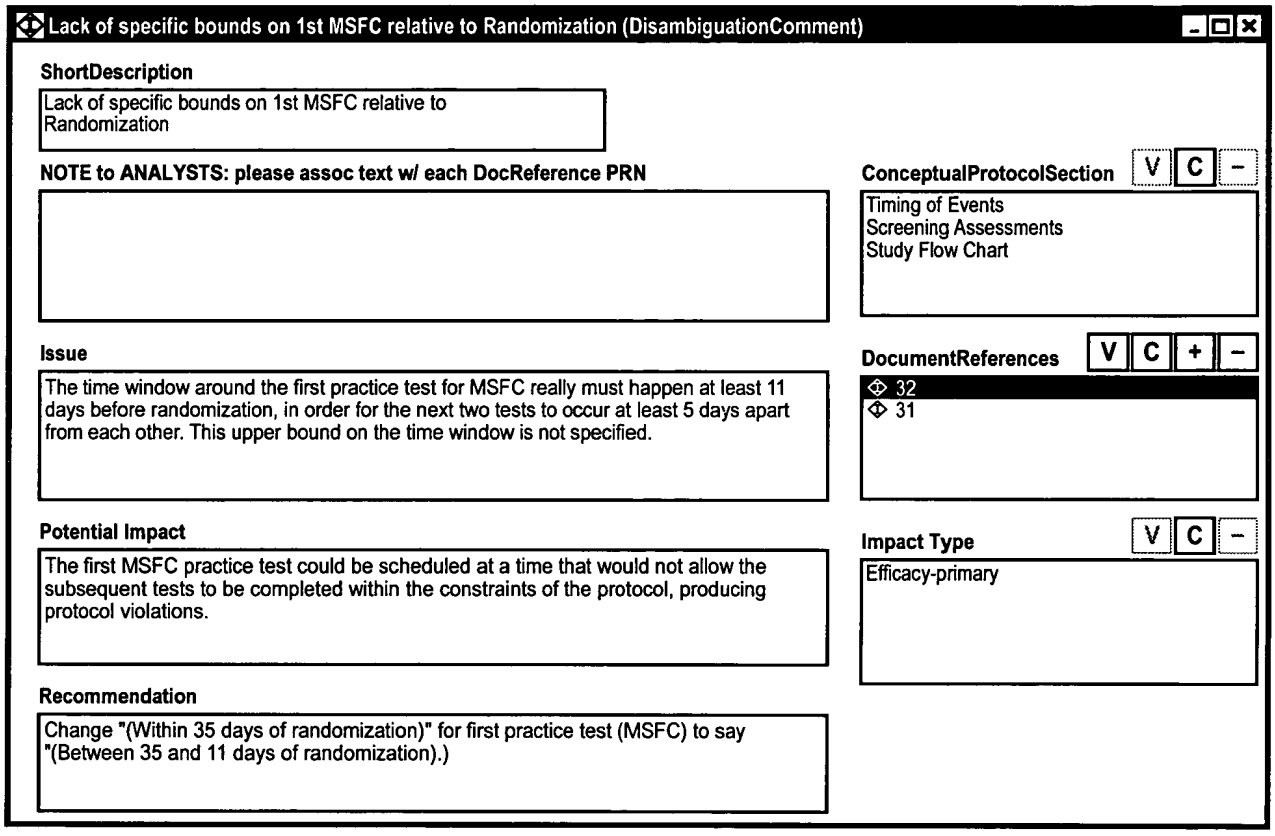
Lack of specific bounds on 1st MSFC relative to Randomization (DisambiguationComment)
ShortDescription
Lack of specific bounds on 1st MSFC relative to Randomization
NOTE to ANALYSTS: please assoc text w/ each DocReference PRN
ConceptualProtocolSection
V C -
Timing of Events
Screening Assessments
Study Flow Chart
Issue
The time window around the first practice test for MSFC really must happen at least 11 days before randomization, in order for the next two tests to occur at least 5 days apart from each other. This upper bound on the time window is not specified.
DocumentReferences
V C + -
32
31
Potential Impact
The first MSFC practice test could be scheduled at a time that would not allow the subsequent tests to be completed within the constraints of the protocol, producing protocol violations.
Impact Type
V C -
Efficacy-primary
Recommendation
Change "(Within 35 days of randomization)" for first practice test (MSFC) to say "(Between 35 and 11 days of randomization).)

FIG. 34

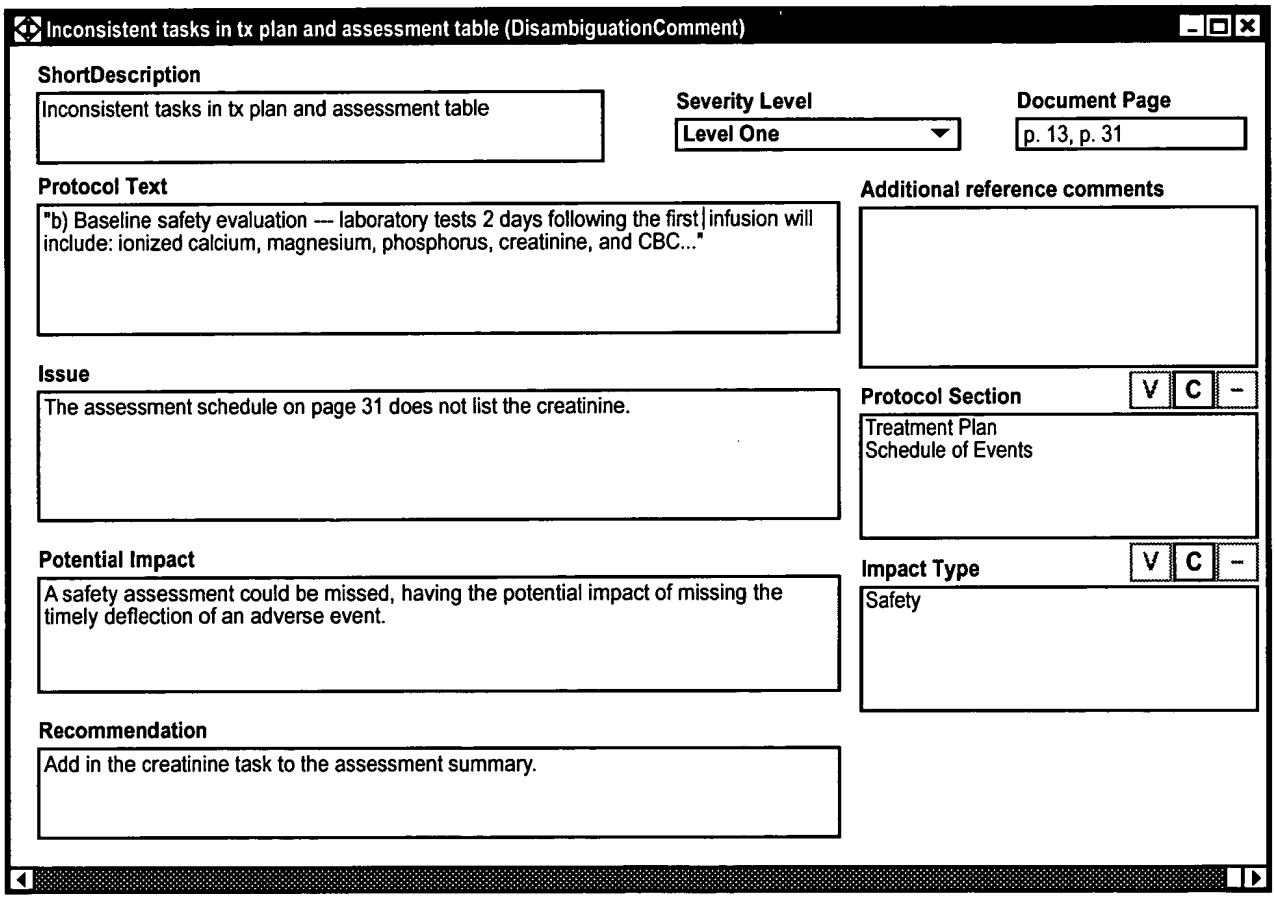
Inconsistent tasks in tx plan and assessment table (DisambiguationComment)
ShortDescription
Inconsistent tasks in tx plan and assessment table
Severity Level
Level One
Document Page
p. 13, p. 31
Protocol Text
"b) Baseline safety evaluation --- laboratory tests 2 days following the first infusion will include: ionized calcium, magnesium, phosphorus, creatinine, and CBC..."
Additional reference comments
Issue
The assessment schedule on page 31 does not list the creatinine.
Protocol Section
V C -
Treatment Plan
Schedule of Events
Potential Impact
A safety assessment could be missed, having the potential impact of missing the timely deflection of an adverse event.
Impact Type
V C -
Safety
Recommendation
Add in the creatinine task to the assessment summary.

FIG. 35

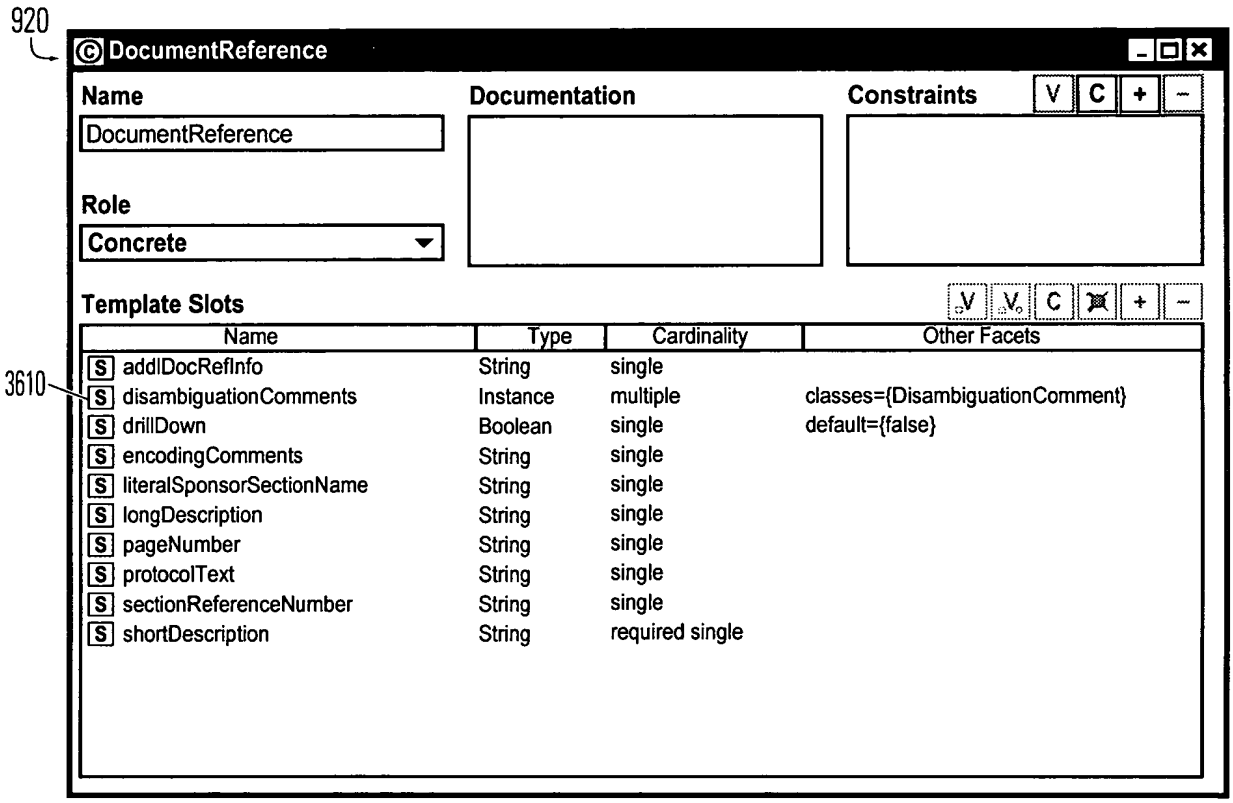
920
DocumentReference
Name
DocumentReference
Role
Concrete
Documentation
Constraints
V
C
+
–
Template Slots
Name
Type
Cardinality
Other Facets
3610
addlDocRefInfo String single
disambiguationComments Instance multiple classes={DisambiguationComment}
drillDown Boolean single default={false}
encodingComments String single
literalSponsorSectionName String single
longDescription String single
pageNumber String single
protocolText String single
sectionReferenceNumber String single
shortDescription String required single

FIG. 36

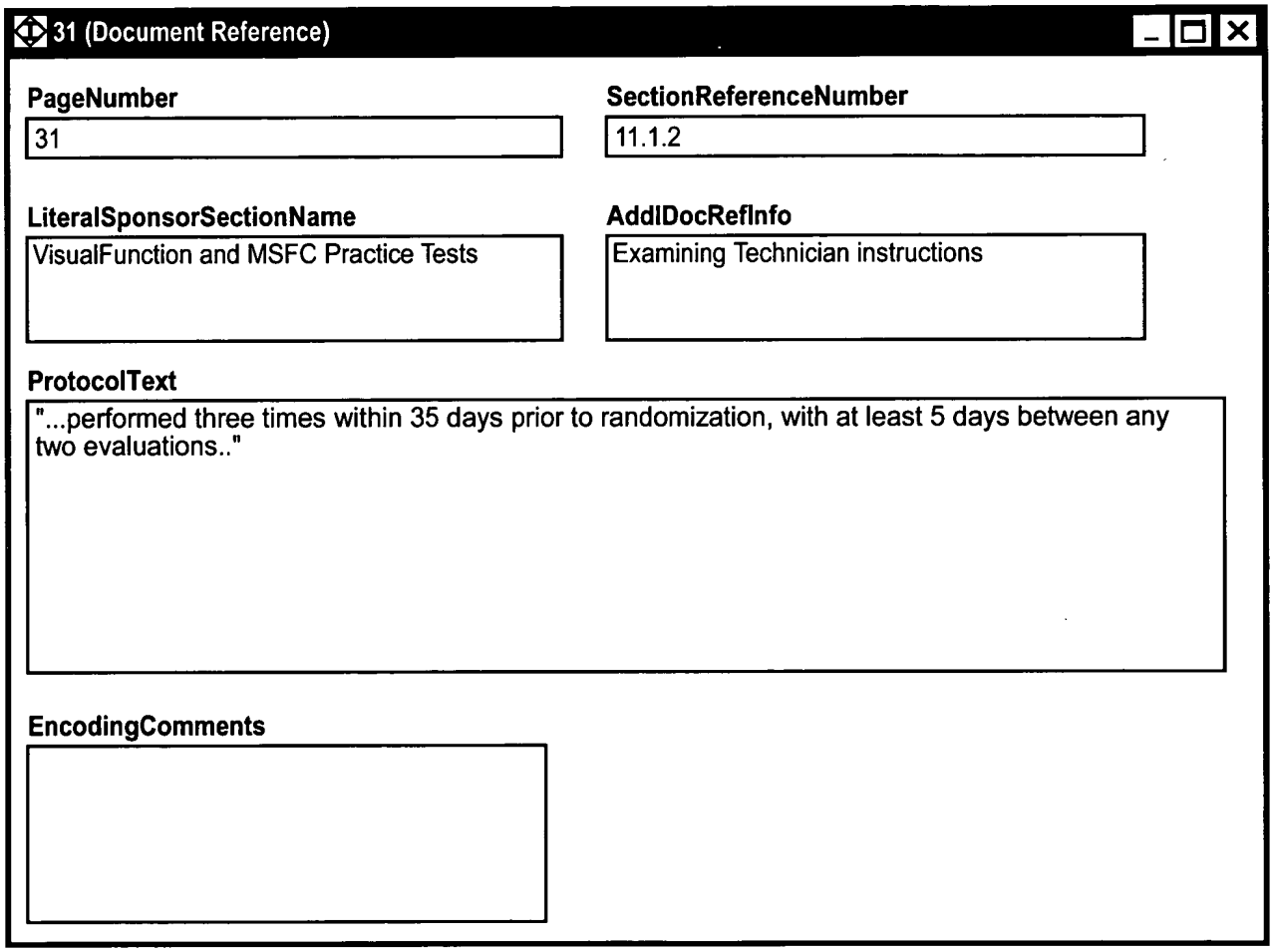
31 (Document Reference)
PageNumber
31
SectionReferenceNumber
11.1.2
LiteralSponsorSectionName
VisualFunction and MSFC Practice Tests
AddlDocRefInfo
Examining Technician instructions
ProtocolText
"...performed three times within 35 days prior to randomization, with at least 5 days between any two evaluations.."
EncodingComments

FIG. 37

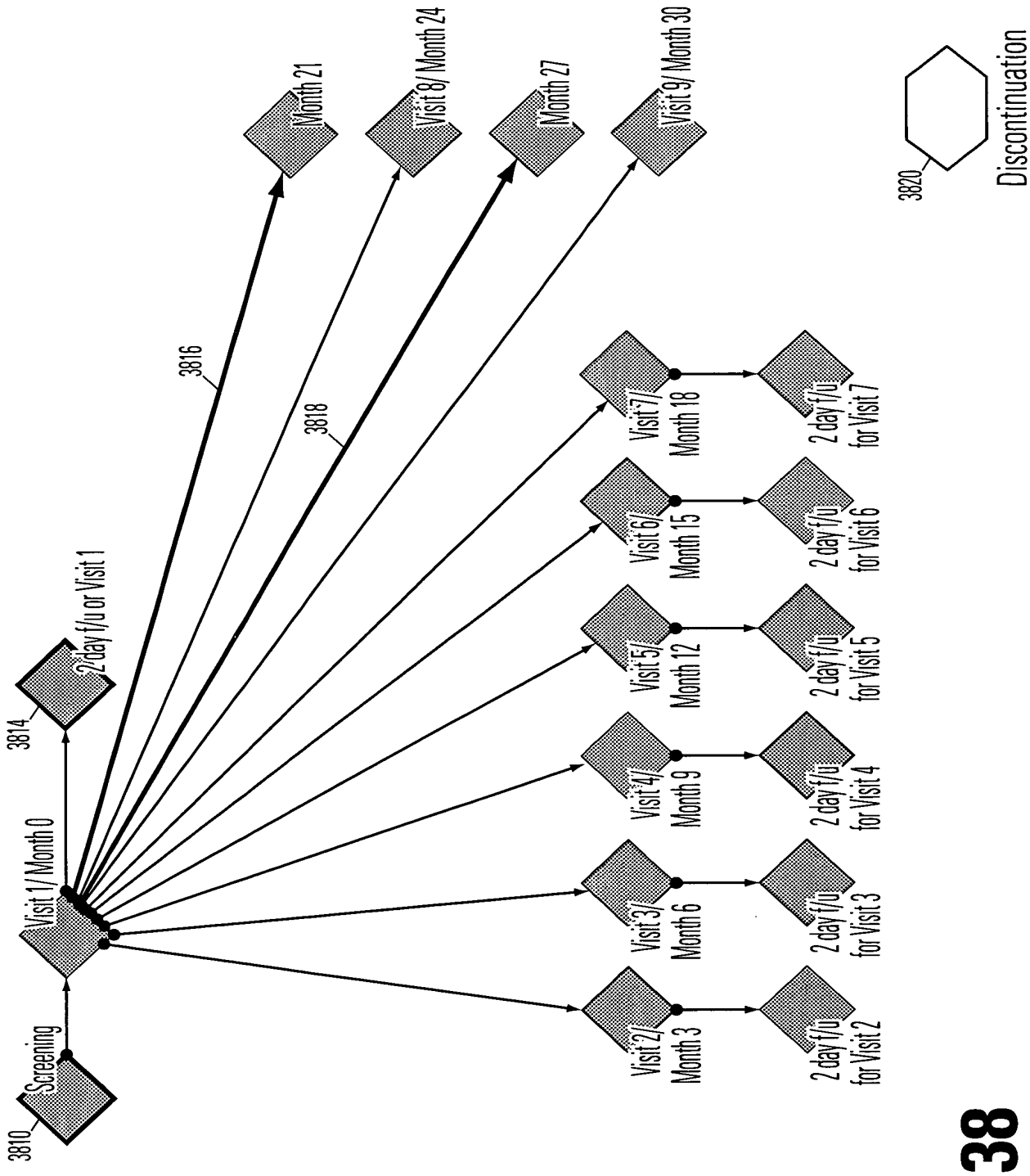
Screening
3810
Visit 1/ Month 0
2/day f/u or Visit 1
3814
3816
3818
Visit 2/ Month 3
Visit 3/ Month 6
Visit 4/ Month 9
Visit 5/ Month 12
Visit 6/ Month 15
Visit 7/ Month 18
Month 21
Visit 8/ Month 24
Month 27
Visit 9/ Month 30
2 day f/u for Visit 2
2 day f/u for Visit 3
2 day f/u for Visit 4
2 day f/u for Visit 5
2 day f/u for Visit 6
2 day f/u for Visit 7
3820
Discontinuation

FIG. 38

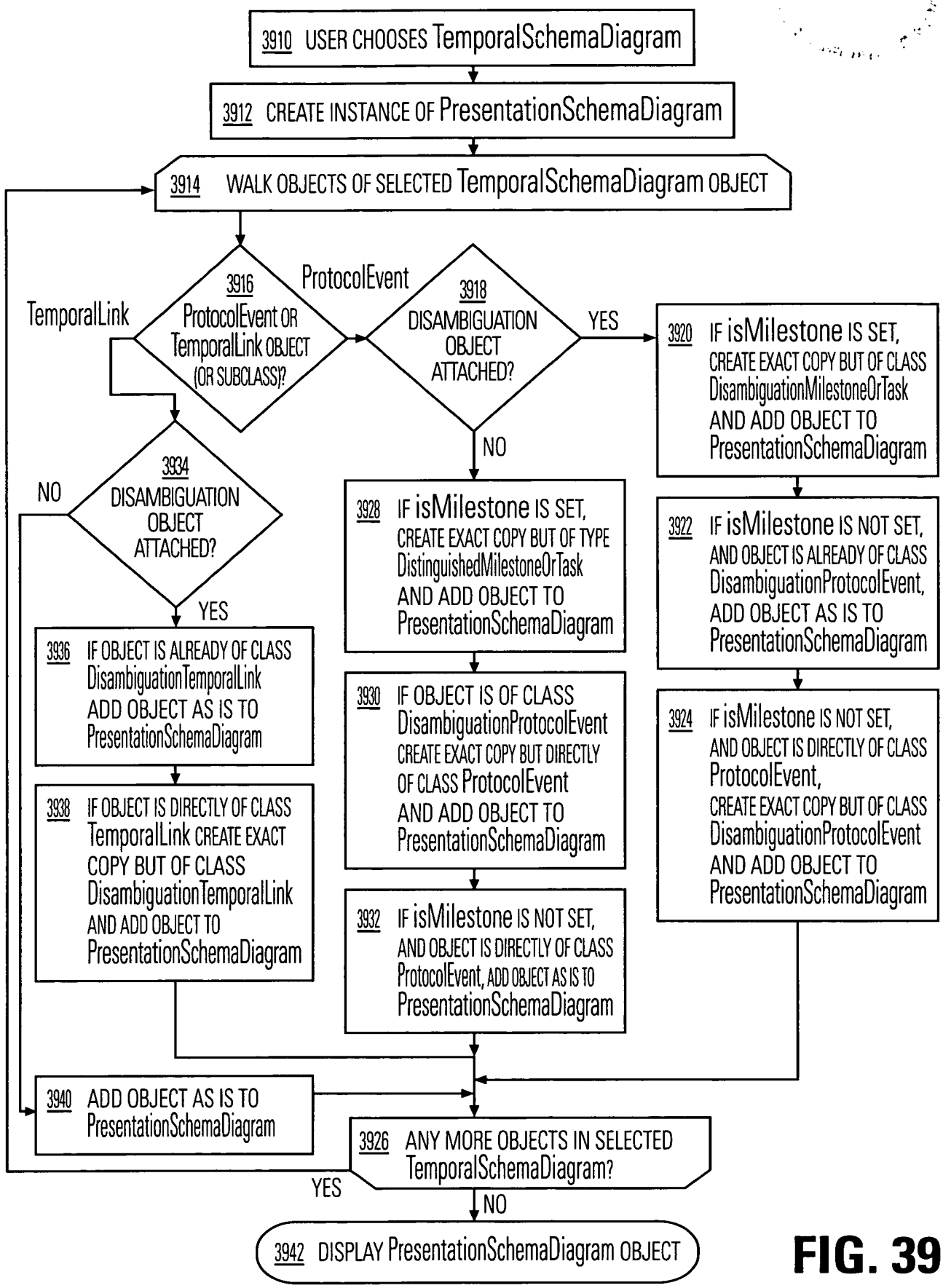

FIG. 39

DISAMBIGUATION FINDINGS

Item	Impact Type	Protocol Section	Description	Document Reference
1	Safety Efficacy-primary Efficacy-secondary	Protocol Summary Study Flow Chart	**Issue:** The description in the Protocol Synopsis of when assessments should be performed after 16 weeks is not consistent with Appendix I Schedule of Assessments. **Potential Impact:** Confusion as to when to perform these evaluations (clinical parameters and safety assessments) could result in inconsistent and inaccurate collection of data for the study. **Recommendation:** Revise sentence in the Protocol Synopsis to read, "After 16 weeks these evaluations will be performed every two to "four" months..." in order to be consistent with the timepoints indicated in Appendix I Schedule of Assessments.	*Pg. 12; Section Protocol Synopsis; Procedure; Paragraph 6:* "Clinical parameters (ACR core set) and safety assessments (adverse events and laboratory parameters) will be performed at baseline and then at monthly intervals up to 16 weeks. After 16 weeks these evaluations will be performed every two to three months, up to 104 weeks."

FIG. 40

Item	Impact Type	Protocol Section	Description	Document Reference
4	Safety Accrual	Screening Assessments Study Flow Chart	**Issue:** The protocol text specifies that if an analysis with evidence of seropositivity was performed within 6 months before screening, then rheumatoid factor testing will not have to be performed at screening. However, this is not noted in Appendix I Schedule of Assessments. **Potential Impact:** Unnecessary analysis performed at screening. **Recommendation:** Add a footnote to the Rheumatoid Factor assessment in Appendix I to clarify that documented evidence of seropositivity is acceptable as screening data if obtained within 6 months before screening.	*Pg. 28; Section 8.6.2; Rheumatoid Factor:* "Unless there is documented evidence of rheumatoid factor titre within 6 months before screening a blood sample for this analysis will be taken." *Pg. 41; Section Appendix I; Schedule of Assessments*

FIG. 41